



US007879334B1

(12) **United States Patent**
Saxon et al.

(10) **Patent No.:** **US 7,879,334 B1**
(45) **Date of Patent:** **Feb. 1, 2011**

(54) **FUSION MOLECULES AND TREATMENT OF IGE-MEDIATED ALLERGIC DISEASES**

(75) Inventors: **Andrew Saxon**, Santa Monica, CA (US); **Ke Zhang**, Los Angeles, CA (US); **Daocheng Zhu**, Los Angeles, CA (US)

(73) Assignee: **The Regents of the University of California**, Oakland, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **11/799,442**

(22) Filed: **Apr. 30, 2007**

Related U.S. Application Data

(63) Continuation of application No. 09/847,208, filed on May 1, 2001, now Pat. No. 7,265,208.

(51) **Int. Cl.**
C07K 16/46 (2006.01)
A61K 39/00 (2006.01)
A61K 39/35 (2006.01)
A61K 39/36 (2006.01)

(52) **U.S. Cl.** **424/185.1**; 424/134.1; 424/192.1; 424/275.1; 530/350

(58) **Field of Classification Search** None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,902,495 A 2/1990 Kaliner et al.
5,017,693 A 5/1991 Hylarides et al.
5,116,964 A 5/1992 Capon et al.
5,141,648 A 8/1992 Hylarides et al.
5,329,028 A 7/1994 Ashkenazi et al.
5,336,603 A 8/1994 Capon et al. 435/69.7
5,358,710 A 10/1994 Sehon et al.
5,420,247 A 5/1995 Gearing et al.
5,512,283 A 4/1996 Byers et al.
5,558,869 A 9/1996 Burks, Jr. et al.
5,560,915 A 10/1996 Patterson et al.
5,563,250 A 10/1996 Hylarides et al.
5,565,335 A 10/1996 Capon et al.
5,637,454 A 6/1997 Harley
5,645,820 A 7/1997 Hafler et al.
5,672,683 A 9/1997 Friden et al.
5,698,679 A * 12/1997 Nemazee 530/387.3
5,736,507 A 4/1998 Boots et al.
5,811,265 A 9/1998 Quertermous et al.
5,817,308 A * 10/1998 Scott et al. 424/93.21
5,827,516 A 10/1998 Urban et al.
5,843,449 A 12/1998 Boots et al.
5,858,980 A 1/1999 Weiner 514/13
5,869,093 A 2/1999 Weiner et al.
5,880,103 A 3/1999 Urban et al.
5,925,351 A 7/1999 Browning et al. 424/143.1
5,945,294 A 8/1999 Frank et al.
5,965,605 A 10/1999 Cheng et al.
5,973,121 A 10/1999 Burks et al.
5,977,307 A 11/1999 Friden et al.
6,043,345 A 3/2000 Saxon et al.

6,093,699 A 7/2000 Sehon et al.
6,103,697 A 8/2000 Bergstrand et al.
6,214,974 B1 4/2001 Rosenblum et al.
6,228,373 B1 5/2001 Bergstrand et al.
6,228,374 B1 5/2001 Bergstrand et al.
6,287,792 B1 9/2001 Pardridge et al.
6,372,250 B1 4/2002 Pardridge et al.
7,101,581 B2 * 9/2006 Ehrman 426/392
7,265,208 B2 * 9/2007 Saxon et al. 530/387.1
7,488,804 B2 * 2/2009 Saxon et al. 530/387.3
7,534,440 B2 * 5/2009 Saxon 424/192.1
2001/0053770 A1 12/2001 Thomas et al.
2003/0049237 A1 3/2003 Bannon et al.
2003/0077282 A1 4/2003 Bigler et al.
2004/0198961 A1 10/2004 An et al.
2005/0250934 A1 11/2005 Wang et al.
2006/0171942 A1 * 8/2006 Saxon et al. 424/133.1
2009/0136493 A1 * 5/2009 Saxon et al. 424/133.1
2009/0317389 A1 * 12/2009 Saxon 424/134.1

FOREIGN PATENT DOCUMENTS

WO WO 88/09344 * 12/1988

(Continued)

OTHER PUBLICATIONS

Fasler et al., *J. Allergy and Clinical Immunology* 101(4 pt 1): 521-30, Apr. 1998.*
Burks et al., *Eur. J Biochem* 245: 334-339; 1997.*
Stanley et al., *Archives of Biochemistry and Biophysics* 342(2): 244-253; 1997.*
Daeron et al., *J Clin Invest* 95(2): 577-85, Feb. 1995.*
Rafnar et al., *J Biol Chem* 266(2): 1229-1236, 1991.*
Terada et al., *Clinical Immunology* 120(1): 45-56, 2006.*
Tangley et al., *A therapy for cat allergies, Thanks to mice, the New York time*, pp. 1-2, Apr. 5, 2005.*
Saxon et al., *J Allergy Clin Immunol* 121: 320-325, 2008.*
Zhang et al., *Immunol Allergy Clin North Am* 27(1): 93-103, Feb. 2007.*
Zhu et al., *Nat Med* 11(4): 446-449, Epub Mar. 27, 2005.*
Krauss et al., *Eur. J. Immunol.*, 25(1): pp. 192-199 (1995).
Basu et al., *The Journal of Biological Chemistry*, 268(18): pp. 13118-13127 (1993).
New Riverside University Dictionary, Boston, MA, pp. 933 (1994).
Ngo et al., *The Protein Folding Problem and Tertiary Structure Prediction*, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495 (1994).

(Continued)

Primary Examiner—Phuong Huynh
(74) *Attorney, Agent, or Firm*—James A. Fox; Ginger R. Dreger; Arnold & Porter LLP

(57) **ABSTRACT**

The invention concerns bifunctional fusion molecules for the treatment of IgE-mediated allergic conditions and FcεRI-mediated autoimmune conditions. The invention provides a new therapeutic approach for the treatment of both acute and late-phase allergic responses due to ingestion, inhalation, cutaneous and parenteral exposure to allergens, responses including asthma, allergic rhinitis, atopic dermatitis, severe food allergies, chronic urticaria and angioedema, as well as anaphylactic reactions due to exposures such as bee stings or penicillin allergy. In addition, the invention provides for a novel, safer and more efficacious form of allergy vaccination.

24 Claims, 11 Drawing Sheets

FOREIGN PATENT DOCUMENTS

WO	WO 95/14779	6/1995
WO	WO 95/26365	10/1995
WO	WO 96/26961	* 2/1996
WO	WO 96/12740	5/1996
WO	WO 96/16086	5/1996
WO	WO 96/22024	7/1996
WO	WO 96/26961	9/1996
WO	WO 96/40789	12/1996
WO	WO 99/02709	1/1999
WO	WO 99/02710	1/1999
WO	WO 99/02711	1/1999
WO	WO 99/57241	11/1999
WO	WO 99/67293	12/1999
WO	WO 00/05254	2/2000
WO	WO 02/102320 A2	12/2002
WO	WO 02/102320 A3	12/2002

OTHER PUBLICATIONS

- Skolnick et al., *Trends in Biotech.*, 18(1): pp. 34-39 (2000).
- Tao et al., *The Journal of Immunology*, 143(8): pp. 2595-2601 (1989).
- Zhu et al., *Nature Medicine*, 1219: pp. 1-4 (2005).
- Allen, L., et al., "Modifications to an Fc γ -Fc ϵ Fusion Protein Alter Its Effectiveness in the Inhibition of Fc ϵ RI-Mediated Functions," *J. Allergy Clin. Immunol.*, 120: 462-468, 2007.
- Terada, T., et al., "A Chimeric Human-Cat Fc γ -Fel d1 Fusion Protein Inhibits Systemic, Pulmonary, and Cutaneous Allergic Reactivity to Intratracheal Challenge in Mice Sensitized to Fel D1, the Major Cat Allergen," *Clinical Immunology*, 4C: 1-12, 2006.
- Zhang, Ke, et al., "Chimeric Human Fc γ -Allergen Fusion Proteins in the Prevention of Allergy," *Immunol. Allergy Clin. N. Am.*, 27: 93-103, 2007.
- Zhu, D. et al., "A Chimeric Human-Cat Fusion Protein Blocks Cat-Induced Allergy," *Nature Medicine*, pp. 1-4, 2005.
- "alpha β -Crystallin in Multiple Sclerosis", *J. Immunol.*, vol. 129-135, pp. 1-5, Jul. 20, 2001 (<http://www.albany.net/~tjc/crystalline.html>).
- "Autoantigen Sequences", pp. 1-3, Jul. 11, 2001 (http://129.206.51.31/mb/ana_base.html).
- "Autoimmune Disease: Rapid Progress in our Understanding of Immune Function Promises More Effective Treatments for Autoimmune Disorders", *Nature Biotechnology*, vol. 18, pp. IT7-IT9, Supplement 2000.
- "Histones and Subclasses", Jul. 30, 2001, Purified Antigens for Autoimmune Testing, (<http://www.immunovision.com/pg0019.htm>).
- Abdelilah, S.G., et al., "Molecular Characterization of the Low-Affinity IgE Receptor Fc EpsilonRII/CD23 Expressed by Human Eosinophils", *Int Immunol.*, Apr. 1998; 10(4):395-404.
- Abramson, M.J., et al., "Allergen immunotherapy for asthma", *The Cochrane Library*, Jan. 1998; 1:1-32.
- Adamczewski, M., and Kinet, J.P., "The High-Affinity Receptor for Immunoglobulin E" *Chemical Immunol.*, 59:173-190(1994).
- Akdis, C., et al., Epitope-Specific T Cell Tolerance to Phospholipase A₂ in Bee Venom Immunotherapy and Recovery by IL-2 and IL-15 In Vitro, *The American Society for Clinical Investigations, Inc.*, vol. 98(7), pp. 1676-1683, 1996.
- Alvarez-Fernandez, Marcia, et al., "Inhibition of Mammalian Legumain by Some Cystatins is Due to a Novel Second Reactive Site", *The Journal of Biological Chemistry*, vol. 274, No. 27, Issue of Jul. 2, pp. 19195-19203, 1999.
- American Autoimmune Related Diseases Association, Questions and Answers, pp. 1-4, Jul. 26, 2001 (http://www.aarda.org/questions_and_answers.html).
- Ansari, AA, et al., "Epitope Mapping of the Branched Chain Alpha-Ketoacid Dehydrogenase Dihydrolipoyl Transacylase (BCKD-E2) Protein that Reacts with Sera from Patients with Idiopathic Dilated Cardiomyopathy", (abstract), *J Immunol.*, 153(10):4754-65, Nov. 15, 1994.
- Antoniou, A. N., et al., "Control of Antigen Presentation by a Single Protease Cleavage Site", *Immunity*, vol. 12, pp. 391-398, Apr. 2000.
- Arm et al., "Molecular Cloning of gp49, a Cell-surface Antigen That is Preferentially Expressed by Mouse Mast Cell Progenitors and is a New Member of the Immunoglobulin Superfamily" *J. Biol. Chem.* 266:15966-73 (1991).
- Arm, J.P., et al., "Molecular Identification of a Novel Family of Human Ig Superfamily Members That Possess Immunoreceptor Tyrosine-Based Inhibition Motifs and Homology to the Mouse gp49B1 Inhibitory Receptor^{1, 2}", *J. Immunol.*, vol. 159, pp. 2342-2349, 1997.
- AroTec Diagnostics Limited—Jo-1 Antigen, pp. 1-2, Jul. 11, 2001 (<http://webnz.com/arotec/masa5005.htm>).
- AroTec Diagnostics Limited—La (SSB) Antigen, pp. 1-3, Jul. 12, 2001 (<http://webnz.com/arotec/masa5010.htm>).
- AroTec Diagnostics Limited—Myeloperoxidase (pANCA) Antigen, pp. 1-3, Jul. 12, 2001. (<http://webnz.com/arotec/masa5009.htm>).
- AroTec Diagnostics Limited—Parietal Cell Antigen (H/K-ATPase), pp. 1-3, Jul. 12, 2001 (<http://webnz.com/arotec/masa5004.htm>).
- AroTec Diagnostics Limited—Proteinase 3 (cANCA) Antigen, pp. 1-3, Jul. 12, 2001 (<http://webnz.com/arotec/masa5008.htm>).
- AroTec Diagnostics Limited—RNP/Sm Antigen, pp. 1-3, Jul. 12, 2001 (<http://webnz.com/arotec/masa5006.htm>).
- AroTec Diagnostics Limited—Ro (SSA) Antigen, pp. 1-3, Jul. 11, 2001 (<http://webnz.com/arotec/masa5011.htm>).
- AroTec Diagnostics Limited—Scl-70 Antigen, pp. 1-3, Jul. 12, 2001 (<http://webnz.com/arotec/masa5001.htm>).
- AroTec Diagnostics Limited—Sm Antigen, pp. 1-3, Jul. 12, 2001 (<http://webnz.com/arotec/masa5007.htm>).
- AroTec Diagnostics Limited— β 2-Glycoprotein 1 (human), pp. 1-3, Jul. 12, 2001 (<http://webnz.com/arotec/masa5002.htm>).
- Ashman, Robert F., et al., "Fc Receptor Off Signal in the B Cell Involves Apoptosis", *The Journal of Immunology*, vol. 157, pp. 5-11, 1996.
- Atwood, T. K., et al., "The Babel of Bioinformatics", *Science*, vol. 290, No. 5491, pp. 471-473, Oct. 2000.
- Auto Immune, Inc., "Overview of Oral tolerance Therapy" Research and Development—OT Technology, Jul. 30, 2001, (http://www.autoimmuneinc.com/R_D/tech.html).
- Bajramovic, JJ, et al., "Presentation of α B-Crystallin to T Cells in Active Multiple Sclerosis Lesions: An Early Event Following Inflammatory Demyelination", *The American Association of Immunologists*, vol. 164, pp. 4359-4366, 2000.
- Barker RN, et al., "Red Blood Cell Glycophorins as B and T-cell Antigens in Canine Autoimmune Haemolytic Anaemia", (abstract) *Vet Immunol Immunopathol.*, 47(3-4):225-38, Aug. 1995.
- Barnes, Peter, "Anti-IgE Antibody Therapy for Asthma" *The New England Journal of Medicine* 341:2006-2008 (1999).
- Beasley et al., "prevalence and Etiology of asthma" *J. Allergy Clin. Immunol.* 105:466-472 (2000).
- Bellmann, K., et al., "Potential risk of oral insulin with adjuvant for the prevention of Type I diabetes: a protocol effective in NOD mice may exacerbate disease in BB rats", *Diabetologia*, vol. 41, pp. 844-847, 1998.
- Bielekova, B., et al., "Encephalitogenic potential of the myelin basic protein peptide (amino acids 83-99) in multiple sclerosis: results of a phase II clinical trial with an altered peptide ligand", *Nat Med.*, vol. 6, No. 10, pp. 1167-1175, Oct. 2000.
- Bigazzi, PE, MD, Lecture on "Autoimmune Disease", *The University of Connecticut*, pp. 1-6, Jul. 30, 2001, (<http://155.37.1.60/Lectures/PB/Autoimmune.html>).
- Blanas, E. et al., "Induction of Autoimmune Diabetes by Oral Administration of Autoantigen", *Science*, vol. 274, pp. 1707-1709, Dec. 6, 1996.
- Blondel, A. and Bedouelle, "Engineering the quaternary structure of an exported protein with a leucine zipper" *Protein Engineering* 4:457-461 (1991).
- Bonfa, E., et al., "Frequency and Epitope Recognition of Anti-Ribosome P Antibodies from Humans with Systemic Lupus Erythematosus and MRL/lpr Mice are Similar", (abstract), *J Immunol.*; 140(1):3434-3437, May 15, 1998.
- Borel, et al., "A Novel Technique to Link either Proteins or Peptides to Gammaglobulin to Construct Tolerogens" *J. of Immun. Methods*, vol. 126, pp. 159-168 (1990).

- Borel, et al., "Oligonucleotide Linked to Human Gammaglobulin Specifically Diminishes Anti-DNA Antibody Formation in Cultured Lymphoid Cells from Patients with Systemic Lupus Erythematosus" *J. Clin. Invest.*, vol. 82, pp. 1901-1907 (1988).
- Bowie, James U., et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions", *Science*, vol. 247, pp. 1306-1310, Mar. 16, 1990.
- Boyce and Austen, "No Audible Wheezing: Nuggets and Conundrums from Mouse Asthma Models," *JEM*, 201:(12) 1869-1873 (2005).
- Brazis, P., et al., "Stem cell factor enhances IgE-mediated histamine and TNF- α release from dispersed canine cutaneous mast cells", *Vet Immunol Immunopathol*, Jun. 30, 2000; 75(1-2):97-108.
- Breiteneder, H, PhD, et al., "Complementary DNA cloning and expression in *Escherichia coli* of Aln g I, the major allergen in pollen of alder (*Alnus glutinosa*)", *J Allergy Clin. Immunol.*, vol. 90, No. 6, pp. 909-917, 1992.
- Bridges, S. L., Jr., MD, PhD, et al., "T-cell Receptor Peptide Vaccination in the Treatment of Rheumatoid Arthritis", *Emerging Therapies for Rheumatoid Arthritis*, vol. 24, No. 3, pp. 641-651, 1998.
- Bridges, SL, Jr., et al., "T-Cell Receptor Peptide Vaccination in the Treatment of Rheumatoid Arthritis", *Emerging Therapies for Rheumatoid Arthritis*, vol. 24, pp. 641-650, 1998.
- Burks, et al. "Mapping and mutational analysis of the IgE-binding epitopes on Ara h 1, a legume vicilin and a major allergen in peanut hypersensitivity" *Eur. J. Biochem.* 245:334-339 (1997).
- Cambier, J.C., "Inhibitory receptors abound?" *Proc. Natl. Acad. Sci. USA* 94:5992-5995 (1997).
- Cambier, JC, "Commentary: Inhibitory receptors abound?", *Proc. Natl. Acad. Sci. USA*, vol. 94, pp. 5993-5995, 1997.
- Campbell, K.A., "Co-crosslinking Fc epsilon RII/CD23 and B cell surface immunoglobulin modulates B cell activation", *Eur J. Immunol* Aug. 1992; 22(8):2107-12.
- Casares et al. "Engineering an characterization of a murine MGC class II-immunoglobulin chimera expressing an immunodominant CD4 T viral epitope" *Protein Engineering* 10(11):1295-1301 (1997).
- Casares et al., "Antigen-specific Signaling by a Soluble, Dimeric Peptide/Major Histocompatibility Complex Class II/Fc Chimera Leading to T helper Cell Type 2 Differentiation" *J. Ex. Med.* 190:543-553 (Nov. 1999).
- Cascio P, et al., "26Sproteasomes and Immunoproteasomes Produce Mainly N-Extended Cersions of an Antigenic Peptide", *EMBO J*, 20(10):2357-2366, May 15, 2001, (abstract).
- Castells, M., "Mast Cells: Molecular and Cell Biology", *The Journal of Asthma, Allergy and Immunology*, vol. 1N1:1-17, 1999.
- Chaillous, L, et al., "Combined analysis of islet cell antibodies which cross-react with mouse pancreas, antibodies to the M, 64,000 islet protein, and antibodies to glutamate decarboxylase in subjects at risk for IDDM", *Diabetologia*, vol. 37, pp. 491-499, 1994.
- Chaillous, L. et al., "Oral insulin administration and residual β -cell function in recent-onset type 1 diabetes: a multicentre randomized controlled trial", *The Lancet*, vol. 356, pp. 545-549, 2000.
- Chan and Sinclair, "Regulation of the Immune Response" *Immunology* 21:967-981 (1971).
- Chapman, Martin D., et al., "Recombinant Allergens for Diagnosis and Therapy of Allergic Disease", *J Allergy Clin Immunol*, pp. 409-418, 2000.
- Coffman and Hessel, "Nonhuman Primate Models of Asthma," *JEM*, 201:(12) 1875-1879 (2005).
- Costa et al., "The IgE-binding epitopes of rPar j2, a major allergen of *Parietaria judaica* pollen, are heterogeneously recognized among allergic subjects" *Allergy* 55:246-50 (2000).
- Couzin, J., et al., "Diabetes' Brave New World", *Science*, vol. 300, pp. 1862-1865, Jun. 2003.
- Critchfield, JM, et al., "T Cell Deletion in High Antigen Dose Therapy of Autoimmune Encephalomyelitis", *Science* Feb. 25; 263(5150):1139-43, 1994 (abstract).
- Cunningham, Brian C., et al., "High-Resolution Epitope Mapping of hGH-Receptor Interactions by Alanine-Scanning Mutagenesis", *Science*, vol. 244, pp. 1081-1085, Jun. 2, 1989.
- Daëron et al. "The Same Tyrosine-Based Inhibition Motif, in the Intra-cytoplasmic Domain of FC(RIIB, Regulates Negatively BCR-, TCR-, and FcR-Dependent Cell Activation" *Immunity* 3:635-646 (Nov. 1995).
- Daëron et al., "Regulation of High-affinity IgE Receptor-mediated Mast Cell Activation by Murine Low-affinity IgG₁ Receptors". *J. Clin. Invest* 95:577-585 (Feb. 1995).
- Daëron, et al., *Clin. Invest.*, vol. 95:(2), pp. 577-585 (1995).
- Daëron, Marc, "Fc Receptor Biology," *Annu. Rev. Immunol.* 15-203-2334 (1997).
- Davidson, A., et al, "Autoimmune Diseases", *N. Engl. J. Med.*, vol. 345, No. 5, pp. 340-350, Aug. 2, 2001.
- De Lara, J.M. Tunon, "Immunoglobulines E et cellules de l'inflammation" *Rev. Mal. Resp.* 13:27-36 (1996).
- De Palma, R, et al., "Use of Altered Peptide Ligands to Modulate Immune Responses as a Possible Immunotherapy for Allergies", *Allergy*: 55: Suppl 61: 56-59, 2000.
- Decker, Patrice, et al., "Inhibition of Caspase-3-Mediated Poly (ADP-Ribose) Polymerase (PARP) Apoptotic Cleavage by Human PARP Autoantibodies and Effect on Cells Undergoing Apoptosis", *The Journal of Biological Chemistry*, © 2000 by The American Society for Biochemistry and Molecular Biology, Inc., vol. 275, No. 12, pp. 9043-9046, Mar. 24, 2000.
- Delespesse, G., et al., "The Low-Affinity Receptor for IgE," *Immunol. Rev.*, vol. 125, pp. 77-97, Feb. 1992.
- Dieterich, W., et al., Identification of Tissue Transglutaminase as the Autoantigen of Celiac Disease, *Nat Med*; 3(7):797-801, Jul. 1997 (abstract).
- Ditzel, Henrik J., "Human Antibodies in Cancer and Autoimmune Disease", *Immunologic Research*; 21(2-3):185-193, 2000.
- Dombrowicz, D., et al., "Anaphylaxis Mediated Through a Humanized High Affinity IgE Receptor", *The Journal of Immunology*, vol. 157, pp. 1645-1651, 1996.
- Earnshaw WC, et al., "Identification of a Family of Human Centromere Proteins Using Autoimmune Sera From Patients With Scleroderma", (abstract) *Chromosoma*, 91(3-4):313-321, 1985.
- Elias et al., Post translational Addition of an Argine Moiety to Acidic NH₂ Termini of Proteins is Required for Their Recognition by Ubiquitin-Protein Ligase, *J. Biol. Chem.*, vol. 265, No. 26, pp. 15511-15517, Sep. 1990.
- Elkon, KB, et al., "Lupus Autoantibodies Target Ribosomal P Proteins", (abstract) *J Exp Med*, 162(2): 459-471, Aug. 1, 1985.
- Ellison and Hood., "Linkage and sequence homology of two human immunoglobulin (heavy chain constant region genes" *Proc. Nat. Acad. Sci. USA* 79:1984-1988 (1982).
- Ellison et al., "The nucleotide sequence of a human immunoglobulin c(1 gene" *Nucl. Acids Res.* 10(13):4071-4079 (1982).
- Fabien N., et al., "Autoantibodies Directed Against the Ribosomal P Proteins are not Only Directed Against A Common Epitope of the P0, P1 and P2 Proteins", (abstract) *J Autoimmune*, 13(1): 103-110, Aug. 1999.
- Faria AM, et al., "Oral Tolerance: Mechanisms and Therapeutic Applications", (abstract), *Adv Immunol*, 73:153-264, 1999.
- Fiebiger E., et al., "Cytokines Regulate Proteolysis in Major Histocompatibility complex Class II-Dependent Antigen Presentation by Dendritic Cells" *J. Exp. Med.*, 193(8):881-892, Apr. 16, 2001, (abstract).
- Fiebiger et al., "Anti-Fc ϵ RI α Autoantibodies in Autoimmune-mediated Disorders Identification of a StructureFunction Relationship" *J. Clin. Invest.* 101:243-251 (Jan. 1998).
- Fiebiger et al., "Serum IgG Autoantibodies Directed against the α Chain of a Fc ϵ RI: A Selective Marker and Pathogenic Factor for a Distinct Subset of Chronic Urticaria Patients" *The Journal of Clinical Investigation* 96:2006-2612 (Dec. 1995).
- Frampton, G., et al., "Identification of Candidate Endothelial Cell Autoantigens in Systemic Lupus Erythematosus Using a Molecular Cloning Strategy: A Role for Ribosomal P Protein P0 as an Endothelial Cell Autoantigen", *Rheumatology (Oxford)*, (abstract) 39(10):1114-1120, Oct. 2000.
- Fridman, W., "Fc Receptors and Immunoglobulin binding factors" *FASEB J.*, 5(12):2684-90 (1991).

- Gerber, Jeffrey and Mosser, David, "Reversing Lipopolysaccharide Toxicity by Ligating the Macrophage Fc ϵ Receptors" *The Journal of Immunology* 6861-6868 (2001).
- Germain, R.N., "The T Cell Receptor for Antigen: Signaling and Ligand Discrimination", *The Journal of Biological Chemistry*, vol. 276, No. 38, pp. 35223-35226, Jul. 2, 2001.
- Giovannoni, G., et al., "Multiple Sclerosis and its Treatment", (abstract) *J R Coll Physicians Lond*, 33(4):315-22, Jul.-Aug. 1999.
- Gold, D. P., et al., "T-Cell Receptor Peptides as Immunotherapy for Autoimmune Disease", *Critical ReviewsTM In Immunology*, vol. 17, pp. 507-510, 1997.
- Gold, Daniel P., et al., "T-Cell Receptor Peptides as Immunotherapy for Autoimmune Disease", *Critical ReviewsTM In Immunology*, (abstract) 17:507-510, 1997.
- Gold, DP, "Results of a Phase I Clinical Trial of a T-Cell Receptor Vaccine in Patients with Multiple Sclerosis. II. Comparative Analysis of TCR Utilization in CSF T-Cell Populations Before and After Vaccination with a TCRV Beta 6 CDR2 Peptide", (abstract) *J Neuroimmunol*, 76(1-2):29-38, Jul. 1997.
- Gold, HA, et al., "The RNA Processing Enzyme RNase MRP is Identical to the Th RNP and Related to RNase P", (abstract) *Science*, 245(4924):1377-80, Sep. 22, 1989.
- Gollnick et al., "Isolation, Characterization, and Expression of Cdna Clones Encoding the Mouse Fc Receptor for IgE (Fc ϵ RII)" *The Journal of Immunology* 144:1974-1982 (1974).
- Goodkin, D. E., et al., "A phase I trial of solubilized DR2:MBP⁸⁴⁻¹⁰² (AG284) in multiple sclerosis", *Neurology*, vol. 54, pp. 1414-1420, 2000.
- Gottlieb, A.B., et al., Anti-CD4 Monoclonal Antibody Treatment of Moderate to Severe Psoriasis Vulgaris: Results of a Pilot, Multicenter, Multiple-Dose, Placebo-Controlled Study, (abstract) *J Am Acad Dermatol*, 43(4):595-604, Oct. 2000.
- Gunnarsson, Andreas, et al., "Molecular Properties of the Goodpasture Epitope", *The Journal of Biological Chemistry*, vol. 275, No. 40, pp. 30844-30848, Oct. 6, 2000.
- Guo, C.B., et al., "Identification of IgE-bearing cells in the late-phase response to antigen in the lungs as basophils", *Am J Respir Cell Mol Biol.*, Apr. 1994; 10(4):384-90.
- Harrison, L.C. and Hafler, D.A., "Antigen-Specific Therapy for Autoimmune Disease," *Current Opinion in Immunology*, vol. 12, pp. 704-711, 2000.
- Haselden, B. M., et al., "Immunoglobulin E-Independent Major Histocompatibility Complex-Restricted T Cell Peptide Epitope-induced Late Asthmatic Reactions", *J. Exp. Med.*, vol. 189, No. 12, pp. 1885-1894, Jun. 21, 1999.
- Haselden, B.M., et al., "Peptide-Mediated Immune Responses in Specific Immunotherapy", *Int Arch Allergy Immunol*, 122(4):229-37, 2000.
- Hayami et al., "Molecular Cloning of a Novel Murine Cell-surface Glycoprotein Homologous to Killer Cell Inhibitory Receptors" *J. Biol. Chem.* 272:7320-7 (1997).
- Hellman, Lars, "Characterization of four novel ϵ chain of mRNA and a comparative analysis of genes for immunoglobulin E in rodents and man". *Eur. J. Immunol.* 23:159-167 (1993).
- Hellmark, T., et al., "Characterization of Anti-GBM Antibodies Involved in Goodpasture's Syndrome", (abstract) *Kidney Int*, 46(3):823-9, Sep. 1994.
- Helm, B. A., et al., "Identification of the High Affinity Receptor Binding Region in Human Immunoglobulin E", *The Journal of Biological Chemistry*, vol. 271, No. 13, Issue of Mar. 29, pp. 7494-7500, 1996.
- Henz, B.M., et al., [Urticaria. New developments and perspectives], *Hautarzt* May 2000;51(5):302-8.
- Hide et al., "Autoantibodies against the high-affinity IgE receptor as a cause of histamine release in chronic urticaria" *N. Engl. J. Med.* 328:1599-1604 (1993).
- Hirano, T., et al., "Human Tissue Distribution of TA02, which is Homologous with a New Type of Aspartic Proteinase, Napsin A", (abstract) *Jpn J Cancer Res*, 91(10):1015-21, Oct. 2000.
- Hughes, G.R., *The Antiphospholipid Syndrome: Ten Years On*, (abstract) *Lancet*, 342(8867):341-344, Aug. 7, 1993.
- Hulett, Mark D., et al., "Fine Structure Analysis of Interaction of Fc ϵ RI with IgE", *Journal of Biological Chemistry*, vol. 274, No. 19:13345-13352, 1999.
- Immunovision (Brochure), "PCNA Antigen", Purified Antigens for Autoimmune Testing, Jul. 30, 2001, (<http://www.immunovision.com/pg0061.htm>).
- Immunovision (Brochure), "La/SS-B", Purified Antigens for Autoimmune Testing, (<http://www.immunovision.com/pg0014.htm>), Jul. 30, 2001.
- Immunovision (Brochure), "Mitochondrial Antigen", Purified Antigens for Autoimmune Testing, (<http://www.immunovision.com/pg0020.htm>), Jul. 30, 2001.
- Immunovision (Brochure), "Ribosomal P Antigen", Purified Antigens for Autoimmune Testing, Jul. 30, 2001, (<http://www.immunovision.com/pg0021.htm>).
- Immunovision (Brochure), "Ro/SS-A Antigen", Jul. 30, 2001, (<http://www.immunovision.com/pg0013.htm>).
- Immunovision (Brochure), "Scl-70 Antigen", Purified Antigens for Autoimmune Testing (<http://www.immunovision.com/pg0017.htm>), Jul. 30, 2001.
- Immunovision (Brochure), "Smith (sm) Antigen", Purified Antigens for Autoimmune Testing (<http://www.immunovision.com/pg0015.htm>), Jul. 30, 2001.
- Ji, Tae H., et al., "Bifunctional Reagents", *Methods of Enzymology*, vol. 91, pp. 581-609, 1983.
- Kabat, *Sequences of Proteins of Immunological Interest* Voll III Fifth Ed. (1991).
- Kaplan, A.P., "Urticaria and Angioedema," *Inflammation: Basic Principles and Clinical Correlates*, (Gallin and Snyderman eds.), 3rd Edition, Lippincott & Wilkins, Philadelphia, 1999, pp. 915-928.
- Kaplan, Allen P., "Urticaria and Angioedema" *Inflammation: Basic Principles and Clinical Correlates* Gallin and Snyderman Eds., Chapter 35:667-678 Raven press, NY (1998).
- Kappos, L., et al., "Induction of a non-encephalitogenic type 2 T helper-cell autoimmune response in multiple sclerosis after administration of an altered peptide ligand in a placebo-controlled, randomized phase II trial", *Nature Medicine*, vol. 6, No. 10, pp. 1176-1182, Oct. 2000.
- Karlsson, F.A., et al., "Major Parietal Cell Antigen in Autoimmune Gastritis with Pernicious Anemia is the acid-producing H⁺, K⁺-adenosine Triphosphatase of the Stomach", (Abstract) *J Clin Invest*, 81(2):475-9, Feb. 1988.
- Katz, Howard R., "gp49BE and its Related Family of Counterregulatory Receptors of the Immunoglobulin Superfamily", *Int. Arch. Allergy Immunol.* 118:177-179 (1999).
- Kawabori, S., et al., "Existence of c-kit receptor-positive, tryptase-negative, IgE-neg cells in human allergic nasal mucosa: a candidate for mast cell progenitor", *Int. Arch Allergy Immunol.* Jan. 1997;112(1):36-43.
- Kepley, C.L., et al., "Purification of human basophils by density and size alone", *J. Immunol. Meth.*, 175:1-9, 1994.
- Kepley, C.L., et al., "The identification and characterization of umbilical cord-blood derived basophils", *J. Leukocyte Biol.*, 64:474-483, 1998.
- Kepley, C.L., et al., "The identification and partial characterization of a unique marker for human basophils", *J. Immunol.*, 154, 6548-6555, 1995.
- Kepley, et al., "Fc ϵ RI-Fc γ RII Coaggregation inhibits IL-16 production from human langerhans-like dendritic cells", *Clinical Immunology*, 108: 89-94 (2003).
- Kikutani et al. "Molecular Structure of Human Lymphocyte Receptor for Immunoglobulin E" *Cell* 47:657-665 (Dec. 1996).
- Kikutani, H., et al., "Molecular structure of human lymphocyte receptor for immunoglobulin E", *Cell* Dec. 5, 1986;47(5):657-65.
- Kinet, J-P, "The High-Affinity IGE Receptor (Fc ϵ RI): From Physiology to Pathology", *Annu. Rev. Immunol.*, vol. 17, pp. 931-972, 1999.
- Kisseley, A. F., "Proteasome Active Sites Allosterically Regulate Each Other, Suggesting a Cylindrical Bite-Chew Mechanism for Protein Breakdown", *Molecular Cell*, vol. 4, pp. 395-402, Sep. 1999.
- Kondo et al. "Cloning of cDNAs for New Subtypes of Murine Low-Affinity Tc Receptor for IgE (Fc ϵ RII/CG23)" *Int. Arch. Immunol.* 105:38-48 (1994).

- Kozlowski, Maya, et al., "SHP-1 Binds and Negatively Modulates the c-Kit Receptor by Interaction with Tyrosine 569 in the c-Kit Juxtamembrane Domain", *Molecular and Cellular Biology*, pp. 2089-2099, vol. 18, No. 4, Apr. 1998.
- Krawinkel and Rabbitts, "Comparison of the hinge-coding segments in human immunoglobulin gamma heavy chain genes and the linkage of the gamma 2 and gamma 4 subclass genes" *The EMBO J* 1(4):403-307 (1982).
- Krogsgaard, M., et al., "Visualization of Myelin Basic Protein (MBP) T Cell Epitopes in Multiple Sclerosis Lesions Using a Monoclonal Antibody Specific for the Human Histocompatibility Leukocyte Antigen (HLA)-DR2-MBP 85-99 complex", (abstract), *J Exp Med*, Apr. 17;191(8):1395-412, 2000.
- Kronus, "Addison's Disease", *Enzyme Steroid 21-Hydroxylase (21-OH) Antibody*, (<http://www.kronus.com/products/addisons.html>), Jul. 30, 2001.
- Kronus, "Celiac Disease", *Tissue Transglutaminase (tTg) Autoantibody*, (<http://www.kronus.com/products/ceeliac.html>), Jul. 30, 2001.
- Kronus, "Diabetes", (<http://www.kronus.com/products/diabetes.html>), Jul. 30, 2001.
- Kronus, "Neuromuscular", *Myasthenia Gravis*, (<http://www.kronus.com/products/neuromuscular.html>), Jul. 30, 2001.
- Kronus, "Thyroid Autoimmune", (<http://www.kronus.com/products/thyroid-auto.html>), Jul. 30, 2001.
- Landschulz, W. H., et al., "The Leucine Zipper: A Hypothetical Structure Common to a New Class of DNA Binding Proteins" *Science* 240:1759-1764 (1988).
- Larche, Mark, "Specific Immunotherapy", *British Medical Bulletin*, 56 (No. 4): 1019-1036, 2000.
- Legge et al., "Presentation of a T Cell Receptor Antagonist Peptide by Immunoglobulins Ablates Activation of T Cells by a Synthetic Peptide or Proteins Requiring Endocytic Processing" *J. Ex. Med.* 185(6):1043-1053 (Mar. 1997).
- Legge et al., "Coupling of Peripheral Tolerance to Endogenous Interleukin 10 Promotes Effective Modulation of Myelin-activated T Cells and Ameliorates Experimental Allergic Encephalomyelitis" *J. Ex. Med.* 191(12):2039-2051 (Jun. 2000).
- Liénard, Hélène, et al., "Signal Regulatory Proteins Negatively Regulate Immunoreceptor-dependent Cell Activation", *The Journal of Biological Chemistry*, vol. 274, No. 45, Issue of Nov. 5, pp. 32493-32499, 1999.
- Lin, Shih-Yao, et al., "Giving Inhibitory Receptors a Boost", *Science*, vol. 291, Issue of Jan. 19, pp. 445-446, 2001.
- Luckey, C. J., et al., "Differences in the Expression of Human Class I MHC Alleles and Their Associated Peptides in the Presence of Proteasome Inhibitors", *The Journal of Immunology*, vol. 167, pp. 1212-1221, 2001.
- Ludin et al., "Cloning and expression of the cDNA coding for a human lymphocyte Ige receptor" *EMBO J*. 6:109-114 (1987).
- Lu-Kuo et al., "gp49B1 Inhibitors IgE-initiated Mast Cell Activation through Both Immunoreceptor Tyrosine-based inhibitory Motifs, Recruitment of src Homology 2 Domain-containing Phosphatase-1, and Suppression of Early and Late Calcium Mobilization" *J. Biol. Chem.* 274:5791-96 (1999).
- Lyczak, J. B., et al., "Expression of Novel Secreted Isoforms of Human Immunoglobulin E Proteins", *The Journal of Biological Chemistry*, vol. 271, No. 7, Issue of Feb. 16, pp. 3428-3436, 1996.
- Machiels, J.J., et al. "Complexes of grass pollen allergens and specific antibodies reduce allergic symptoms and inhibit the seasonal increase of IgE antibody", *Clin. Exp. Allergy*, Nov. 20(6); 653-60, 1990.
- Machiels, J.J., et al. "Significant Reduction of Nonspecific Bronchial Reactivity in Patients with Dermatophagoides pteronyssinus-sensitive Allergic Asthma under Therapy with Allergen-Antibody Complexes", *Am. Rev. Respir. Dis.*, vol. 147, pp. 1407-1412, 1993.
- Machiels, J.J., et al., "Allergen-antibody complexes can efficiently prevent seasonal rhinitis and asthma in grass pollen hypersensitive patients", *Allergy*, 1991, 46, 335-348.
- Machiels, J.J., et al., "Allergic Bronchial Asthma Due to Dermatophagoides pteronyssinus Hypersensitivity Can Be Efficiently Treated by Inoculation of Allergen-Antibody Complexes", *J. Clin. Invest.*, vol. 85; Apr. 1990, 1024-1035.
- Malbec and Fridman, "Negative Regulation of Hematopoietic Cell Activation and Proliferation by Fc(RIIB)" *Curr. Top. Microbiol. Immunol.* 244:13-27 (1999).
- Malbec, Odile, et al., "The SH2 Domain-containing Inositol 5-Phosphatase SHIP1 Mediates Cell Cycle Arrest by FcγRIIB", *JBC Papers in Press.*, pp. 1-29, May 18, 2001.
- Manoury B., et al., "An Asparaginyl Endopeptidase Processes a Microbial Antigen for Class II MHC Presentation", *Nature*, 396(6712):625-627, Dec. 17, 1998, (abstract).
- Marks, M. S. et al., "Protein Targeting by Tyrosine- and Di-leucine-based Signals: Evidence for Distinct Saturable Components", *The Journal of Cell Biology*, vol. 135, No. 2, pp. 341-354, Oct. 1996.
- Max et al., "Duplication and Deletion in the Human Immunoglobulin ε Genes" *Cell* 29:691-699 (Jun. 1992).
- McDevitt, H., "Specific Antigen Vaccination to Treat Autoimmune Disease," *PNAS*, vol. 101:(2), pp. 14627-14630 (Oct. 5, 2004).
- McKnight, Steven Lanier, "Molecular Zippers in Gene Regulation", *Scientific American*, pp. 54-64, Apr. 1991.
- McNeil, H. Patrick, et al., "Anti-Phospholipid Antibodies are Directed Against a Complex Antigen that Includes a Lipid-Binding Inhibitor of Coagulation: β₂-Glycoprotein I (apolipoprotein H)", *Proc. Natl. Acad. Sci. USA*, vol. 87, pp. 4120-4124, *Medical Sciences*, Jun. 1990.
- Merck Corp., "Disorders With Type III Hypersensitivity Reactions", *The Merck Manual*, Sec. 12, Ch. 148, *Hypersensitivity Disorders*, Jul. 12, 2001.
- Metcalf et al., "Mast Cells" *Physiological Reviews* 77:1033-1079 (Oct. 1997).
- Metcalf, D.D., et al., "Mast cell ontogeny and apoptosis", *Exp. Dermatol.* 1995; 4:227-230.
- Mikayama, T., et al., "Molecular cloning and functional expression of cDNA encoding glycosylation-inhibiting factor", *Proc. Natl. Acad. Science*, vol. 90, pp. 10056-10060, Nov. 1993.
- Milgro, H., et al., "Treatment of Allergic Asthma with Monoclonal Anti-IgE Antibody", *The New England Journal of Medicine*, vol. 341, No. 26, 1966-1973, 1999.
- Mimori, T., et al., "Characterization of the DNA-binding protein antigen Ku recognized by autoantibodies from Patients with Rheumatic Disorders", (abstract) *J. Biol. Chem.*, 261(5):2274-8, Feb. 15, 1986.
- Minerd, J., "Experimental Therapy Stops Allergic Reactions in Mice", *NIAID News*, 1-2 (May 2002).
- Misaki, Y., et al., "The 56K Autoantigen is Identical to Human Annexin XI", (Abstract) *J. Biol. Chem.*, 269(6):4240-6, Feb. 11, 1994.
- Mocci, S., et al., "The role of autoantigens in autoimmune disease", *Current Opinion in Immunology*, vol. 12, pp. 725-730, 2000.
- Moreland, L. W., et al., "T Cell Receptor Peptide Vaccination in Rheumatoid Arthritis—A Placebo-Controlled Trial Using a Combination of V_β3, V_β14, and V_β17 Peptides", *Arthritis & Rheumatism*, vol. 41, No. 11, pp. 1919-1929, Nov. 1998.
- Moreland, L. W., et al., "V_β17 T Cell Receptor Peptide Vaccination in Rheumatoid Arthritis: Results of Phase I Dose Escalation Study", *The Journal of Rheumatology*, vol. 23, No. 8, pp. 1353-1362, 1966.
- Mu, F.T., et al., "EEA1, an Early Endosome-Associated Protein. EEA1 is a Conserved Alpha-Helical Peripheral Membrane Protein Flanked by Cysteine "Fingers" and Contains a Calmodulin-Binding IQ Motif", *J. Biol. Chem.*, 270(22):13503-11, Jun. 2, 1995.
- Muno D., et al., "Generation of both MHC Class I- and Class II-Restricted Antigenic Peptides from Exogenously Added Ovalbumin in Murin Phagosomes", *FEBS Lett*, 478(1-2):178-182, Jul. 28, 2000, (abstract).
- Mustelin et al., "Lymphocyte Activation: The coming of the protein tyrosine phosphatases" *Front. Biosci.* 3:d 10601096(1998).
- Nakagawa, T., et al., "Immunotherapy of allergic diseases", *Int. Arch. Allergy Immunol* 1993;102(2):117-20.
- Nakajima, Atsuo, et al., "Antigen-Specific T Cell-Mediated Gene Therapy in Collagen-Induced Arthritis", *The Journal of Clinical Investigation*, vol. 107, No. 10, pp. 1293-1301 May 2001.
- Naquet, P., et al., "T Cell Autoreactivity to Insulin in Diabetic and Related Non-Diabetic Individuals", *The Journal of Immunology*, vol. 140, No. 8, pp. 2569-2578, Apr. 15, 1988.

- National Institute of Allergy and Infectious Diseases, Understanding Autoimmune Disease—What are some Examples of Autoimmune Diseases: Rheumatoid Arthritis. (<http://www.niaid.nih.gov/publications/autoimmune/examples.htm>), Jul. 11, 200.
- Nepom, G. T., “Glutamic acid decarboxylase and other autoantigens in IDDM”, *Current Opinion in Immunology*, vol. 7, pp. 825-830, 1995.
- Nepom, G. T., et al., “Identification and modulation of a naturally processed T cell epitope from the diabetes-associated autoantigen human glutamic acid decarboxylase 65 (hGAD65)”, *PNAS*, vol. 98, No. 4, pp. 1763-1768, Feb. 13, 2001.
- Newkirk, Marianna M., et al., “Autoimmune Response to U1 Small Nuclear Ribonucleoprotein (U1 snRNP) Associated with Cytomegalovirus Infection”, *Arthritis Res*, 3: 253-258, Jul. 30, 2001.
- Noel Rose, et al., *The Autoimmune Diseases: Table of Contents, Third Edition*, Academic Press 1998.
- Norman, Philip S., “Therapeutic Potential of Peptides in Allergic Disease”, *Annals of Allergy*, vol. 71, pp. 330-333, Sep. 1993.
- Okano, Y., et al., “Autoantibody to Th Ribonucleoprotein (Nucleolar 7-2 RNA Protein Particle) in Patients with Systemic Sclerosis”, *Arthritis Rheum*, 33(12):1822-8, Dec. 1990, (abstract).
- Oliver, J.M., et al., “Immunologically mediated signaling in basophils and mast cells: finding therapeutic targets for allergic diseases in the human FcεR1 signaling pathway”, *Immunopharmacology* 48, 269-281, 2000.
- Ono, S.J., “Molecular Genetics of Allergic Diseases”, *Annu Rev Immunol*, 18:347-66, 2000, (abstract).
- Osborne, M., et al., “The Inositol 5'-Phosphatase Ship Binds to Immunoreceptor Signaling Motifs and Responds to High Affinity IgE Receptor Aggregation”, *The Journal of Biological Chemistry*, vol. 271, No. 46, Issue of Nov. 15, pp. 29271-29278, 1998.
- O'Shea, E. K. et al., “Evidence That the Leucine Zipper is a Colloid Coil” *Science* 243:38-542 (1989).
- Ota, K., et al., “T-cell recognition of an immunodominant myelin basic protein epitope in multiple sclerosis”, *Nature*, vol. 346, pp. 183-187, Jul. 12, 1990.
- Ott and Cambier, “Activating and inhibitory signaling in mast cells: New opportunities for therapeutic intervention?” *J. Allergy Clin. Immunol.* 106(3):429-440 (2000).
- Pamer, E., et al., “Mechanisms of MHC Class I—Restricted Antigen Processing”, *Annu. Rev. Immunol.*, vol. 16, pp. 323-358, 1998.
- Peat and Li, “Reversing the trend: Reducing the prevalence of asthma” *J. Allergy Clin. Immunol.* 103:1-10 (1999).
- Peng et al., “A New Isoform of Human Membrane-Bound IgE” *Journal of Immunology*. 148:129-136 (Jan. 1992).
- Phillips and Parker, “Cross-Linked of B Lymphocyte Fc(Receptors and Membrane Immunoglobulin Inhibits AntiImmunoglobulin-Induced Blastogenesis” *The Journal of Immunology* 132(2)627-632 (1984).
- Pisetsky, D.S., “The Role of Bacterial DNA in Autoantibody Induction”, (abstract) *Curr Top Microbiol Immunol*, 247:143-155, 2000.
- Pivnyuk, V. I., et al., “Human Low-Affinity IgE Receptor: cDNA from Cell Line 1B and its Expression in Peripheral Blood Cells”, translated from *Molekulyarnaya Biologiya*, vol. 28, No. 1, pp. 840-845, Jul.-Aug. 1994.
- Pivnyuk, V.I. et al., “Human Low-Affinity IgE Receptor: cDNA from Cell Line 1B and its Expression in Peripheral Blood Cells,” *Molecular Biology*, vol. 28:(4), Part 2, pp. 549-552 (1994).
- Pozzilli, P., et al., “No effect of oral insulin on residual beta-cell function in recent-onset Type I diabetes (the IMDIAB VII)”, *Diabetologia*, vol. 43, pp. 1000-1004, 2000.
- Presta et al., “The Binding Site on Human Immunoglobulin E for its High Affinity Receptor” *J. Biol. Chem.* 269:26368-73 (1994).
- Rabjohn et al., “Molecular cloning and epitope analysis of the peanut allergen Ara h3” *J. Clin. Invest.* 103:535-542 1(1999).
- Resources for Health Professionals: Anaphylaxis, pp. 1-10, Sep. 18, 2001 (http://www.worldallergy.org/professional/allergy_update/anap.../anaphylaxissynopsis.shtm).
- Rickert, M., et al., “Fusion Proteins for Combined Analysis of Autoantibodies to the 65-kda Isoform of Glutamic Acid Decarboxylase and Islet Antigen-2 in Insulin-Dependent Diabetes Mellitus”, *Clin Chem*, 47(5):926-34, May 2001, (abstract).
- Rider, Lisa G., et al., “Laboratory Evaluation of the Inflammatory Myopathies”, *Clinical and Diagnostic Laboratory Immunology*, vol. 2, No. 1, p. 1-9, Jan. 1995.
- Riese, Richard J., et al., “Cathepsin S Activity Regulates Antigen Presentation and Immunity”, *J. Clin. Invest.*, vol. 101, No. 11, 2351-2363, Jun. 1998.
- Rock, K. L., et al., “Degradation of Cell Proteins and the Generation of MHC Class I-Presented Peptides”, *Annu. Rev. Immunol.*, vol. 17, pp. 739-779, 1999.
- Rock, Kenneth L., et al., “Degradation of Cell Proteins and the Generation of MHC Class I-Presented Peptides”, *Annu. Rev. Immunol.*, 17:739-79, 1999, (abstract).
- Rose, N. R., “The Autoimmune Diseases: A Discussion of the Causes and Treatment of Autoimmune Diseases”, *American Autoimmune Related Diseases Associate*, Jul. 26, 2001.
- Ruckert et al. “IL-15-IgG2b fusion protein accelerates and enhances a Th2 but not a Th1 immune response in vivo, while IL-15-IgG2b fusion protein inhibits both” *Eur. J. Inummol.* 28:3312-3320 (1998).
- Saxon et al., “Inhibition of Human IgE Production Via FcεR-II Stimulation Results From a Decrease in the mRNA for Secreted But not Membrane ε H Chains” *The Journal of Immunology* 147:4000-4006 (Dec. 1991).
- Schmidt-Dorr, et al., “Construction, Purification, and Characterization of a Hybrid Protein Comprising the DNA Binding domain of a LexA Repressor and the Jun Leucine Zipper: A Circular Dichroism and Mutagenesis Study”, *Biochemistry* 30:9657-9664 (1991).
- Schuppan, D., et al., “Identification of the Autoantigen of Celiac Disease”, *Ann NY Acad Sci.*, 859:121-6, Nov. 17, 1998, (abstract).
- Schwartz, L., et al., “Development of markers for human basophils and mast cells”, *J. Allergy and Clin. Immunol.*, vol. 94, No. 6, pp. 1231-1240, 1994.
- Sela, M., “Specific Vaccines Against Autoimmune Diseases”, *C R Acad Sci III*; 322(11):933-8, Nov. 1999, (abstract).
- Sharma, S. D., et al., “Antigen-specific therapy of experimental allergic encephalomyelitis by soluble class II major histocompatibility complex—peptide complexes”, *Proc. Natl. Acad. Sci. USA*, vol. 88, pp. 11465-11469, Dec. 1991.
- Shields, et al., “High Resolution Mapping of the Binding Site on Human IgG1 for FcγR1, FcγR2, FcγR3, and FcRn and Design of IgG1 Variants with Improved Binding to the FcγR”, *The Journal of Biological Chemistry*, 276:(9) 6591-6604 (2001).
- Shingo Yabuuchi, et al., “Anti-Cd23 Monoclonal Antibody (IgE Inhibition Involves the Fc Portion of the Molecules”, Abstract 597, *J. Allergy Clin. Immunol.*, vol. 107, No. 2, Feb. 2001.
- Sinclair, N.R. StC., “Why so Many Coinhibitory Receptors?”, *Scand. J. Immunol.*, vol. 50, pp. 1-13, 1999.
- Sinclair, NR, “Why so Many Coinhibitory Receptors?” *Scand. J. Immunol.* 50:10-13 (1999).
- Slidregt, L., et al., “Design and Synthesis of a Multivalent Homing Device for Targeting to Murine CD22”, *Bioorganic & Medicinal Chemistry*, vol. 9, pp. 85-97, 2001.
- Spack, E. G., et al., “Induction of Tolerance in Experimental Autoimmune Myasthenia Gravis with Solubilized MHC Class II: Acetylcholine Receptor Peptide Complexes”, *Journal of Autoimmunity*, vol. 8, pp. 787-807, 1995.
- Stanley et al., “Identification and Mutational Analysis of the Immunodominant IgE Binding Epitopes of the Major Peanut Allergen Ara h 2” *Arch Biochem. Biophys.* 342:244-53 (1997).
- Steinman, L. et al., “Antigen Specific Immunotherapy of Multiple Sclerosis”, *Journal of Clinical Immunology*, vol. 21, No. 2, pp. 93-98, 2001.
- Steinman, L., “Multiple Sclerosis: a Coordinated Immunological Attack Against Myelin in the Central Nervous System”, *Cell*, 85(3):299-302, May 3, 1996, (abstract).
- Steinman, L., et al., “Prospects for Specific Immunotherapy in Myasthenia Gravis” *FASEB J.*; 4(10):2726-31, Jul. 1990, (abstract).
- Stenmark, Harald, et al., “Endosomal Localization of the Autoantigen EEA1 is Mediated by a Zinc-Binding FYVE Finger”, *The Journal of Biological Chemistry*, vol. 271, No. 39, pp. 24048-24054, Sep. 27 1996.
- Stevenson, et al., *J. Immunol.*, vol. 158:5, pp. 2242-2250, Mar. 1997.
- Stoltze L, et al., “Two New Proteases in the MHC Class I Processing Pathway”, *Nat. Immunol.*, 1(5):413-418, Nov. 2000, (abstract).

- Strver, L. et al, *Biochemistry*, Third Edition, W. H. Freeman Company, New York, New York, pp. 31-33, 1998.
- Suter, U., et al., "Expression of human lymphocyte IgE receptor (Fc epsilon RII/CD23). Identification of the Fc epsilon RIIa promoter and functional analysis in B lymphocytes", *J. Immunol.* Nov. 1; 143(9):3087-92, 1989.
- Sutterwala, et al., "Reversal of Proinflammatory Responses by Ligating the Macrophage Fc Receptor Type I" *J. Exp. Med.* 188:217-222 (Jul. 1998).
- Sutterwala, et al., "Selective Suppression of Interleukin-12 induction after Macrophage Receptor Ligation" *J. Exp. Med.* 185:1977-1985 (Jun. 1997).
- Takahashi et al., "Structure of Human Immunoglobulin Gamma Genes Implications for Evolution of a Gene Family" *Cell* 29:671-679 (1982).
- Tan EM, "Antinuclear Antibodies: Diagnostic Markers for Autoimmune Diseases and Probes for Cell Biology", (abstract), *Adv Immunol* 1989, 44:93-151.
- Targoff IN, Autoantibodies to Aminoacyl-Transfer RNA Synthetases for Isoleucine and Glycine. Two Additional Synthetases are Antigenic in Myositis; *J Immunol*, 144(5):1737-1743, Mar. 1, 1990, (abstract).
- TePas, E. C., et al, "Immunotherapy of asthma and allergic diseases", *Current Opinion in Pediatrics*, vol. 12, pp. 574-578, 2000.
- Tisch, R. et al., "Antigen-Specific Mediated Suppression of β Cell Autoimmunity by Plasmid DNA Vaccination," *The Journal of Immunology*, vol. 166, pp. 2122-2132 (2001).
- Tunon, J. M. et al., "Immunoglobines E et cellules de l'inflammation", *Rev. Mal. Resp.*, vol. 13, pp. 27-36, 1996.
- U.S. Department of Health and Human Services, "Sequences of Proteins of Immunological Interest", vol. II and vol. III, Fifth Edition, Table of Contents, pp. iii-xi, 1991.
- Van Rossenberg, S.M., et al, "A Structure-Function Study of Ligand Recognition by CD22 β ", *Journal of Biological Chemistry*, vol. 276, No. 16, Issue of Apr. 20, pp. 12967-12973, 2001.
- Van Venrooij, W.J., Venroij Research Team, Research Topics, General Introduction, "Autoantigens", (abstract), Department of Biochemistry, University of Nijmegen, Jul. 11, 2001.
- Varshavsky, A., "The N-End Rule", vol. 69, pp. 725-735, May 29, 1992.
- Villadangos, J. A., "Proteases involved in MHC class II antigen presentation", *Immunological Reviews*, vol. 172, pp. 109-120, 1999.
- Villadangos, Jose A., "Proteolysis in MHC Class II Antigen Presentation: Who's in Charge?", *Immunity*, vol. 12, pp. 233-239, Mar. 2000.
- Wagtmann et al., "GP49: An Ig-like Receptor with Inhibitory Properties on Mast Cells and Natural Killer Cells" *Current Top. Microbiol. Immunol.* 244:107-113 (1999).
- Wallace, et al., *Methods Enzymol.*, vol. 152, pp. 432-441, 1987.
- Wallner, Barbara P., Short Analytical Review, Peptide Therapy for Treatment of Allergic Diseases, *Clinical Immunology and Immunopathology*, vol. 80, No. 2, Aug., pp. 105-109, 1996.
- Wan, T., et al., "The Crystal Structure of IgE Fc Reveals an Asymmetrically Bent Conformation", *Nature Immunology*, vol. 3, No. 7, pp. 681-686, Jul. 2002.
- Wang, M., et al., "Early IL-4 production driving Th2 differentiation in a human vivo allergic model is mast cell derived", *Immunol.* Jan.;90(1):47-54, 1999.
- Wardrop, III, R.M., et al, Oral Tolerance in the Treatment of Inflammatory Autoimmune Disease, *Inflamm. res.*, 48, pp. 106-119, 1990.
- Warren, K. G., "Increased Synthetic Peptide Specificity of Tissue-CSF Bound Anti-MBP in Multiple Sclerosis", *Journal of Neuroimmunology*, vol. 43, pp. 87-96, (1993).
- Warren, K. G., "Synthetic Peptide Specificity of Anti-Myelin Basic Protein from Multiple Sclerosis Cerebrospinal Fluid", *Journal of Neuroimmunology*, vol. 39, pp. 81-90, (1992).
- Warren, K.G., et al, "Fine Specificity of the Antibody Response to Myelin Basic Protein in the Central Nervous System in Multiple Sclerosis: The Minimal B-Cell Epitope and a Model of its Features", *Proc. Natl. Acad. Sci. USA*, vol. 92, pp. 11061-11065, (Nov. 1995).
- Warren, K.G., et al, "Tolerance Induction to Myelin Basic Protein by Intravenous Synthetic Peptides Containing Epitope P₈₅VVHFFKNIVTP₉₆ in Chronic Progressive Multiple Sclerosis", *Journal of Neurological Sciences*, vol. 152, pp. 31-38, (1997).
- Warren, KG, et al., "Administration of Myelin Basic Protein Synthetic Peptides to Multiple Sclerosis Patients", (abstract), *J. Neurol. Sci.*, vol. 133, No. 1-2, pp. 85-94, Nov. 1995.
- Watson et al., "Molecular cloning and sequencing of the low-affinity IgE receptor (CD23) for horse and cattle" *Vet. Immunol. Immunopathol.* 73:323-9 (2000).
- Watts, C., "Antigen processing in the endocytic compartment", *Current Opinion in Immunology*, vol. 13, pp. 26-31, 2001.
- Watts, C., "Capture and Processing of Exogenous Antigens for Presentation on MHC Molecules", *Annu. Rev. Immunol.*, vol. 15, pp. 821-850, 1997.
- Weiner, H. L., "Double-Blind Pilot Trial of Oral Tolerization with Myelin Antigens in Multiple Sclerosis", *Science*, vol. 259, pp. 1321-1324, (Feb. 26, 1993).
- Wetmur et al., "Kinetics of Renaturation of DNA" *J. Mol. Biol.* 31:349-70 (1966).
- Wetmur, James G., "DNA Probes: Applications of the Principles of Nucleic Acid Hybridization" *Critical Reviews in Biochemistry and Molecular Biology* 26(34):227-59 (1991).
- Wines et al., "The IgG Fc Contains Distinct Fc Receptor (FcR) Binding Sites: The Leukocyte Receptors Fc(RI and Fc(RIIa Bind to a Region in the Fc Distinct from That Recognized by Neonatal FcR and Protein A" *J. Immunol.* 164(10):5313-5318 (2000).
- Wucherpfennig, K. W., et al, "Recognition of the Immunodominant Myelin Basic Protein Peptide by Autoantibodies and HLA-DR2-restricted T Cell Clones from Multiple Sclerosis Patients", *J. Clin. Invest.*, vol. 100, No. 5, pp. 1114-1122, Sep. 1997.
- Yabuuchi, S., et al., "Anti-CD23 Monoclonal Antibody Inhibits Germline κ Transcription in B Cells," *International Immunopharmacology* 2, pp. 453-461, 2002.
- Yamamoto, A.M., et al., "Anti-Titin Antibodies in Myasthenia Gravis: Tight Association with Thymoma of Nonthymoma Patients", *Archives of Neurology*, vol. 58, No. 6, Jun. 2001.
- Yamashita, T., et al., "Expression cloning of complementary DNA encoding three distinct isoforms of guinea pig Fc receptor for IgG1 and IgG2", *J. Immunol.* Aug. 15;151(4) pp. 2014-2023, 1993.
- Yamashita, Y., et al., "Inhibitory and Stimulatory Functions of Paired Ig-Like Receptor (PIR) Family in RBL-2H3 Cells¹", *The Journal of Immunology*, 1998, 161: 4042-4047.
- Yarden et al., "Human proto-oncogene c-kit: a new cell surface receptor tyrosine kinase for an unidentified ligand", *EMBO J.* 6:3341-51 (1987).
- Yewdell, JW., et al., "Not Such a Dismal Science: The Economics of Protein Synthesis, Folding, Degradation and Antigen Processing", *Trends Cell Biol.* 11(7):294-297, Jul. 2001, (abstract).
- Yodoi, J., et al, "Low affinity IgE receptors: regulation and functional roles in cell activation", *Ige, Mast Cells and the Allergic Response*, Wiley Chichester (Ciba Foundation Symposium 147) pp. 133-153, 1989.
- Yoon, J-W., et al, "Control of Autoimmune Diabetes in NOD Mice by GAD Expression or Suppression in β Cells", *Science*, vol. 284, pp. 1183-1187, May 14, 1999.
- Zhang et al., "Two Unusual Forms of Human Immunoglobulin E Encoded by Alternative RNA splicing of ϵ Heavy Chain Membrane Exons", *the Journal of Experimental Med.* 175:233-243 (Jul. 1992).
- Zhu, D., et al., "A novel human immunoglobulin Fc γ -Fc ϵ bifunctional fusion protein inhibits Fc ϵ RI-mediated degranulation", *Nature Medicine*, 8(5) 518-521 (May 2002).
- Zhu, D., et al., "A Novel Human Ig Fc γ -Fc ϵ Chimeric Fusion Protein Inhibits Fc ϵ RI-Mediated Degranulation", (abstract), May 4-7, 2001.
- Zhu, D., et al., "A Novel Ig Fc γ -Fc ϵ Chimeric Fusion Protein Inhibits Fc ϵ RI Mediated Degranulation", Abstract 273, *Clinical Immunology*, vol. 99, No. 1, p. 193, Apr. 19, 2001.

* cited by examiner

FIGURE 1

gagcccaaat cttgtgacaa aactcacaca tgcccaccgt gcccagcacc tgaactcctg 60
gggggaccgt cagtcttctt ctcccccca aaaccaag acaccctcat gatctcccgg 120
accctgagg tcacatgctt ggtggtggac gtgagccacg aagaccctga ggtcaagttc 180
aactggtacg tggacggcgt ggaggtgcat aatgttaaga caaagccgcg ggaggagcag 240
tacaacagca cgtaccgtgt ggtcagcgtc ctaccctcc tgcaccagaa ctggatgaat 300
ggaaaggagt acaagtgcaa ggtctccaac aaagccctcc cagcccccac cgagaaaacc 360
atctccaaag ccaaagtgca gccccgagaa ccacaggtgt acaccctgcc cccatcccgg 420
gatgagctga ccaagaacca ggtcagcctg acctgcctgg tcaaaggctt ctatcccagc 480
gacatcgccg tggagtggga gagcaatggg cagccggaga acaactaaa gaccacgcct 540
cccgtgctgg actccgtcgg ctcttcttc ctctacagca agctcaccgt ggacaagagc 600
aggtggcagc aggggaacgt cttctcatgc tccgtgatgc atgaggctct gcacaaccac 660
taccagcaga ggagcctctc cctgtctccg ggtaaa 696

FIGURE 2

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
Tyr Val Asp Gly Val Glu Val His Asn Val Lys Thr Lys Pro Arg Glu
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
His Gln Asn Trp Met Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Val
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Val Gly Ser Phe Phe
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Gln
Gln Arg Ser Leu Ser Leu Ser Pro Gly Lys

FIGURE 3

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
Asp Gly Val Glu Val His Asn Val Lys Thr Lys Pro Arg Glu Glu Gln
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
Asn Trp Met Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Val Gln Pro
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
Lys Thr Thr Pro Pro Val Leu Asp Ser Val Gly Ser Phe Phe Leu Tyr
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Gln Gln Arg
Ser Leu Ser Leu Ser Pro Gly Lys

FIGURE 4

tccacacaga gcccatccgt cttccccttg acccgctgct gcaaaaacat tccctccaat 60
gccacctccg tgactctggg ctgcctggcc acgggctact tcccggagcc ggtgatggtg 120
acctgggaca caggctccct caacgggaca actatgacct taccagccac caccctcacg 180
ctctctggtc actatgccac catcagcttg ctgaccgtct cgggtgctg ggccaagcag 240
atgttcacct gccgtgtggc acacactcca tcgtccacag actgggtcga caacaaaacc 300
ttcagcgtct gctccagggg cttcaccccc cccaccgtga agatcttaca gtctctctgc 360
gacggcggcg ggcacttccc cccgaccatc cagctcctgt gcctcgtctc tgggtacacc 420
ccagggacta tcaacatcac ctggtctggag gacgggcagg tcatggacgt ggacttgtec 480
accgctcta ccacgcagga ggggtgagctg gcctccacac aaagcgagct caccctcagc 540
cagaagcact ggctgtcaga ccgcacctac acctgccagg tcacctatca aggtcacacc 600
tttgaggaca gcaccaagaa gtgtgcagat tccaaccgga gaggggtgag cgcctaccta 660
agccggccca gcccgctcga cctgttcctc cgcaagtgc ccacgateac ctgtctggtg 720
gtggacctgg caccagcaa ggggaccgtg aacctgacct ggtcccgggc cagtgggaag 780
cctgtgaacc actccaccag aaaggaggag aagcagcgca atggcacgtt aaccgtcacg 840
tccacctgc cgggtgggcac ccgagactgg atcgaggggg agacctacca gtgcagggtg 900
accaccccc acctgccag ggcctcatg cggctcacga ccaagaccag cggcccgcgt 960
gctgccccgg aagtctatgc gtttgcgacg ccggagtggc cggggagccg ggacaagcgc 1020
acctcgcct gcctgatcca gaacttcctg cctgaggaca tctcgggtgca gtggctgcac 1080
aacgaggtgc agtcccggg cgcgccggc agcacgacgc agccccgaa gaccaagggc 1140
tcgggttet tcgtcttcag ccgcctggag gtgaccaggg ccgaatggga gcagaaagat 1200
gagttcatct gccgtgcagt ccatgaggca gcgagccct cacagaccgt ccagcgagcg 1260
gtgtctgtaa atcccggtaa atgacgtact cctgcctccc tccctcccag ggctccatcc 1320
agctgtgcag tggggaggac tggccagacc ttctgtccac tgttgcaatg accccaggaa 1380
gctaccccca ataaactgtg cctgctcaga gccccagtac acccattctt gggagcgggc 1440
agggc 1445

FIGURE 5

Ser Thr Gln Ser Pro Ser Val Phe Pro Leu Thr Arg Cys Cys Lys Asn
Ile Pro Ser Asn Ala Thr Ser Val Thr Leu Gly Cys Leu Ala Thr Gly
Tyr Phe Pro Glu Pro Val Met Val Thr Trp Asp Thr Gly Ser Leu Asn
Gly Thr Thr Met Thr Leu Pro Ala Thr Thr Leu Thr Leu Ser Gly His
Tyr Ala Thr Ile Ser Leu Leu Thr Val Ser Gly Ala Trp Ala Lys Gln
Met Phe Thr Cys Arg Val Ala His Thr Pro Ser Ser Thr Asp Trp Val
Asp Asn Lys Thr Phe Ser Val Cys Ser Arg Asp Phe Thr Pro Pro Thr
Val Lys Ile Leu Gln Ser Ser Cys Asp Gly Gly Gly His Phe Pro Pro
Thr Ile Gln Leu Leu Cys Leu Val Ser Gly Tyr Thr Pro Gly Thr Ile
Asn Ile Thr Trp Leu Glu Asp Gly Gln Val Met Asp Val Asp Leu Ser
Thr Ala Ser Thr Thr Gln Glu Gly Glu Leu Ala Ser Thr Gln Ser Glu
Leu Thr Leu Ser Gln Lys His Trp Leu Ser Asp Arg Thr Tyr Thr Cys
Gln Val Thr Tyr Gln Gly His Thr Phe Glu Asp Ser Thr Lys Lys Cys
Ala Asp Ser Asn Pro Arg Gly Val Ser Ala Tyr Leu Ser Arg Pro Ser
Pro Phe Asp Leu Phe Ile Arg Lys Ser Pro Thr Ile Thr Cys Leu Val
Val Asp Leu Ala Pro Ser Lys Gly Thr Val Asn Leu Thr Trp Ser Arg
Ala Ser Gly Lys Pro Val Asn His Ser Thr Arg Lys Glu Glu Lys Gln
Arg Asn Gly Thr Leu Thr Val Thr Ser Thr Leu Pro Val Gly Thr Arg
Asp Trp Ile Glu Gly Glu Thr Tyr Gln Cys Arg Val Thr His Pro His
Leu Pro Arg Ala Leu Met Arg Ser Thr Thr Lys Thr Ser Gly Pro Arg
Ala Ala Pro Glu Val Tyr Ala Phe Ala Thr Pro Glu Trp Pro Gly Ser
Arg Asp Lys Arg Thr Leu Ala Cys Leu Ile Gln Asn Phe Met Pro Glu
Asp Ile Ser Val Gln Trp Leu His Asn Glu Val Gln Leu Pro Asp Ala
Arg His Ser Thr Thr Gln Pro Arg Lys Thr Lys Gly Ser Gly Phe Phe
Val Phe Ser Arg Leu Glu Val Thr Arg Ala Glu Trp Glu Gln Lys Asp
Glu Phe Ile Cys Arg Ala Val His Glu Ala Ala Ser Pro Ser Gln Thr
Val Gln Arg Ala Val Ser Val Asn Pro Gly Lys

FIGURE 6

Phe Thr Pro Pro Thr Val Lys Ile Leu Gln Ser Ser Cys Asp Gly Gly
Gly His Phe Pro Pro Thr Ile Gln Leu Leu Cys Leu Val Ser Gly Tyr
Thr Pro Gly Thr Ile Asn Ile Thr Trp Leu Glu Asp Gly Gln Val Met
Asp Val Asp Leu Ser Thr Ala Ser Thr Thr Gln Glu Gly Glu Leu Ala
Ser Thr Gln Ser Glu Leu Thr Leu Ser Gln Lys His Trp Leu Ser Asp
Arg Thr Tyr Thr Cys Gln Val Thr Tyr Gln Gly His Thr Phe Glu Asp
Ser Thr Lys Lys Cys Ala Asp Ser Asn Pro Arg Gly Val Ser Ala Tyr
Leu Ser Arg Pro Ser Pro Phe Asp Leu Phe Ile Arg Lys Ser Pro Thr
Ile Thr Cys Leu Val Val Asp Leu Ala Pro Ser Lys Gly Thr Val Asn
Leu Thr Trp Ser Arg Ala Ser Gly Lys Pro Val Asn His Ser Thr Arg
Lys Glu Glu Lys Gln Arg Asn Gly Thr Leu Thr Val Thr Ser Thr Leu
Pro Val Gly Thr Arg Asp Trp Ile Glu Gly Glu Thr Tyr Gln Cys Arg
Val Thr His Pro His Leu Pro Arg Ala Leu Met Arg Ser Thr Thr Lys
Thr Ser Gly Pro Arg Ala Ala Pro Glu Val Tyr Ala Phe Ala Thr Pro
Glu Trp Pro Gly Ser Arg Asp Lys Arg Thr Leu Ala Cys Leu Ile Gln
Asn Phe Met Pro Glu Asp Ile Ser Val Gln Trp Leu His Asn Glu Val
Gln Leu Pro Asp Ala Arg His Ser Thr Thr Gln Pro Arg Lys Thr Lys
Gly Ser Gly Phe Phe Val Phe Ser Arg Leu Glu Val Thr Arg Ala Glu
Trp Glu Gln Lys Asp Glu Phe Ile Cys Arg Ala Val His Glu Ala Ala
Ser Pro Ser Gln Thr Val Gln Arg Ala Val Ser Val Asn Pro Gly Lys

FIGURE 7

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
Asp Gly Val Glu Val His Asn Val Lys Thr Lys Pro Arg Glu Glu Gln
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
Asn Trp Met Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Val Gln Pro
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
Lys Thr Thr Pro Pro Val Leu Asp Ser Val Gly Ser Phe Phe Leu Tyr
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Gln Gln Arg
Ser Leu Ser Leu Ser Pro Gly Lys Val Glu Gly Gly Gly Ser Gly
Gly Gly Gly Ser Gly Gly Gly Gly Ser Phe Thr Pro Pro Thr Val Lys
Ile Leu Gln Ser Ser Cys Asp Gly Gly Gly His Phe Pro Pro Thr Ile
Gln Leu Leu Cys Leu Val Ser Gly Tyr Thr Pro Gly Thr Ile Asn Ile
Thr Trp Leu Glu Asp Gly Gln Val Met Asp Val Asp Leu Ser Thr Ala
Ser Thr Thr Gln Glu Gly Glu Leu Ala Ser Thr Gln Ser Glu Leu Thr
Leu Ser Gln Lys His Trp Leu Ser Asp Arg Thr Tyr Thr Cys Gln Val
Thr Tyr Gln Gly His Thr Phe Glu Asp Ser Thr Lys Lys Cys Ala Asp
Ser Asn Pro Arg Gly Val Ser Ala Tyr Leu Ser Arg Pro Ser Pro Phe
Asp Leu Phe Ile Arg Lys Ser Pro Thr Ile Thr Cys Leu Val Val Asp
Leu Ala Pro Ser Lys Gly Thr Val Asn Leu Thr Trp Ser Arg Ala Ser
Gly Lys Pro Val Asn His Ser Thr Arg Lys Glu Glu Lys Gln Arg Asn
Gly Thr Leu Thr Val Thr Ser Thr Leu Pro Val Gly Thr Arg Asp Trp
Ile Glu Gly Glu Thr Tyr Gln Cys Arg Val Thr His Pro His Leu Pro
Arg Ala Leu Met Arg Ser Thr Thr Lys Thr Ser Gly Pro Arg Ala Ala
Pro Glu Val Tyr Ala Phe Ala Thr Pro Glu Trp Pro Gly Ser Arg Asp
Lys Arg Thr Leu Ala Cys Leu Ile Gln Asn Phe Met Pro Glu Asp Ile
Ser Val Gln Trp Leu His Asn Glu Val Gln Leu Pro Asp Ala Arg His
Ser Thr Thr Gln Pro Arg Lys Thr Lys Gly Ser Gly Phe Phe Val Phe
Ser Arg Leu Glu Val Thr Arg Ala Glu Trp Glu Gln Lys Asp Glu Phe
Ile Cys Arg Ala Val His Glu Ala Ala Ser Pro Ser Gln Thr Val Gln
Arg Ala Val Ser Val Asn Pro Gly Lys

Dose-dependent inhibition of basophil histamine release using the fusion protein GE2 (\pm SEM; n=3 separate donors, each in duplicate)

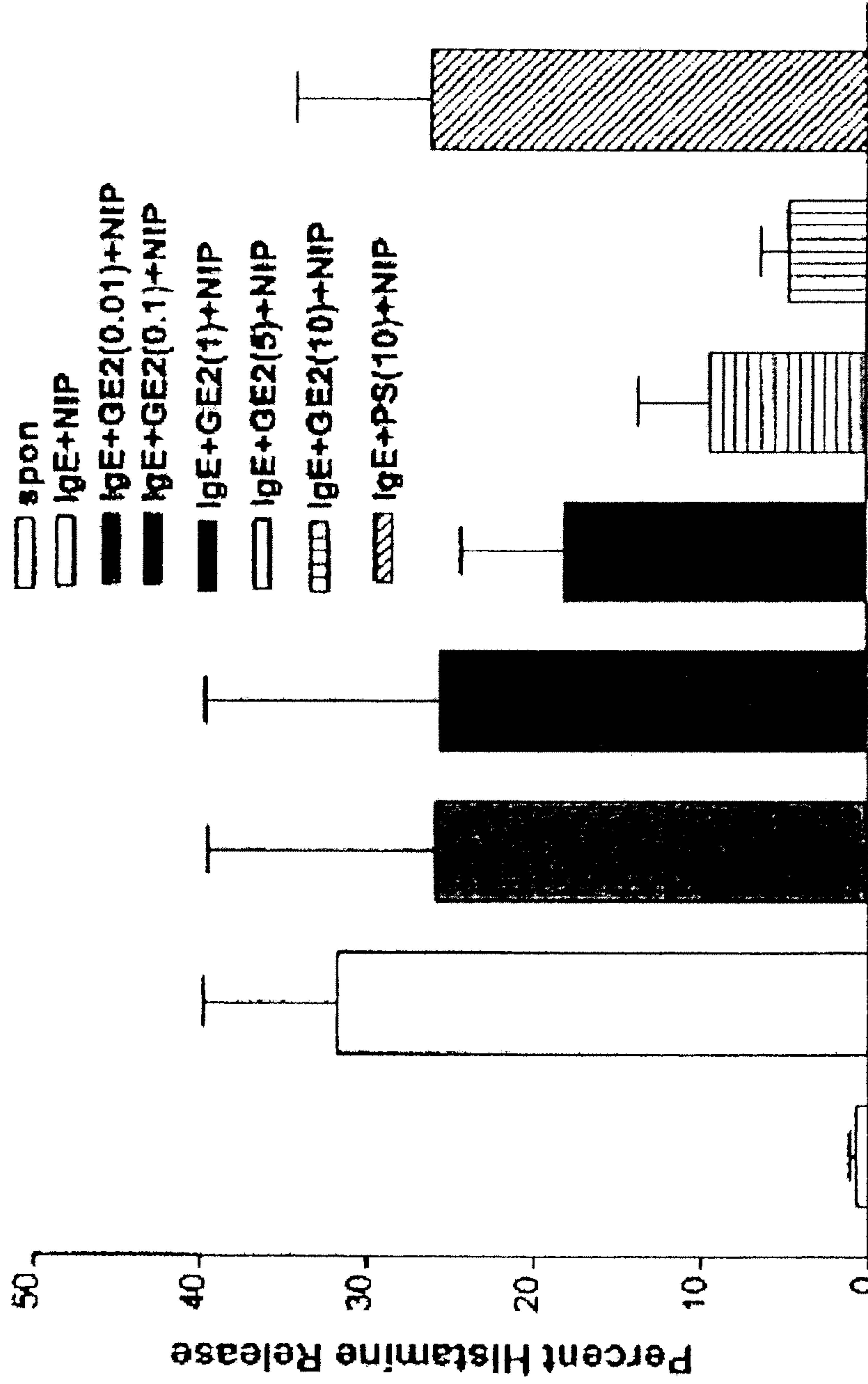
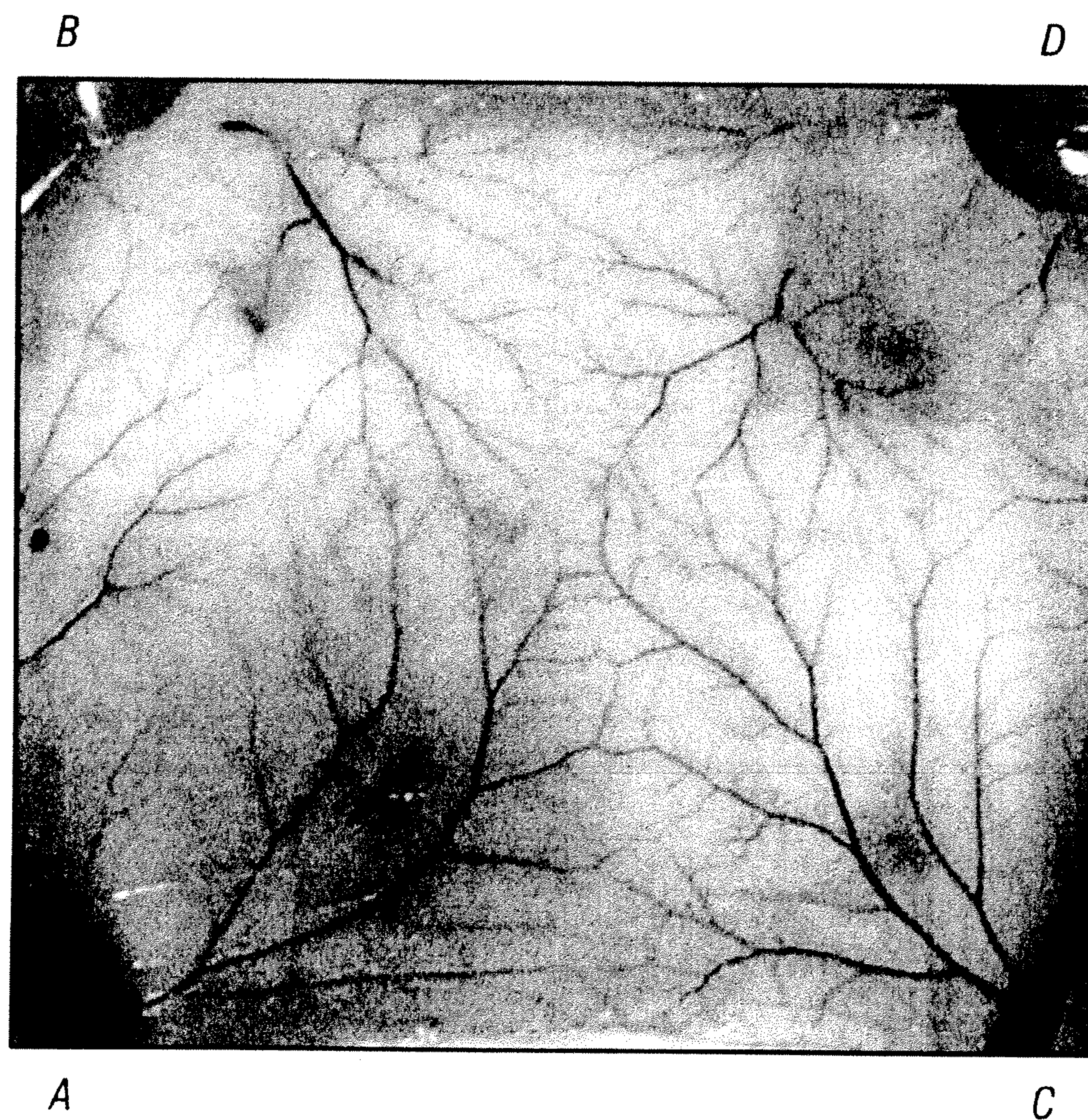


FIGURE 8



A: 250 ng human IgE-anti NP

B: saline

C: 250 nm human IgE-anti NP + 250ng GE2

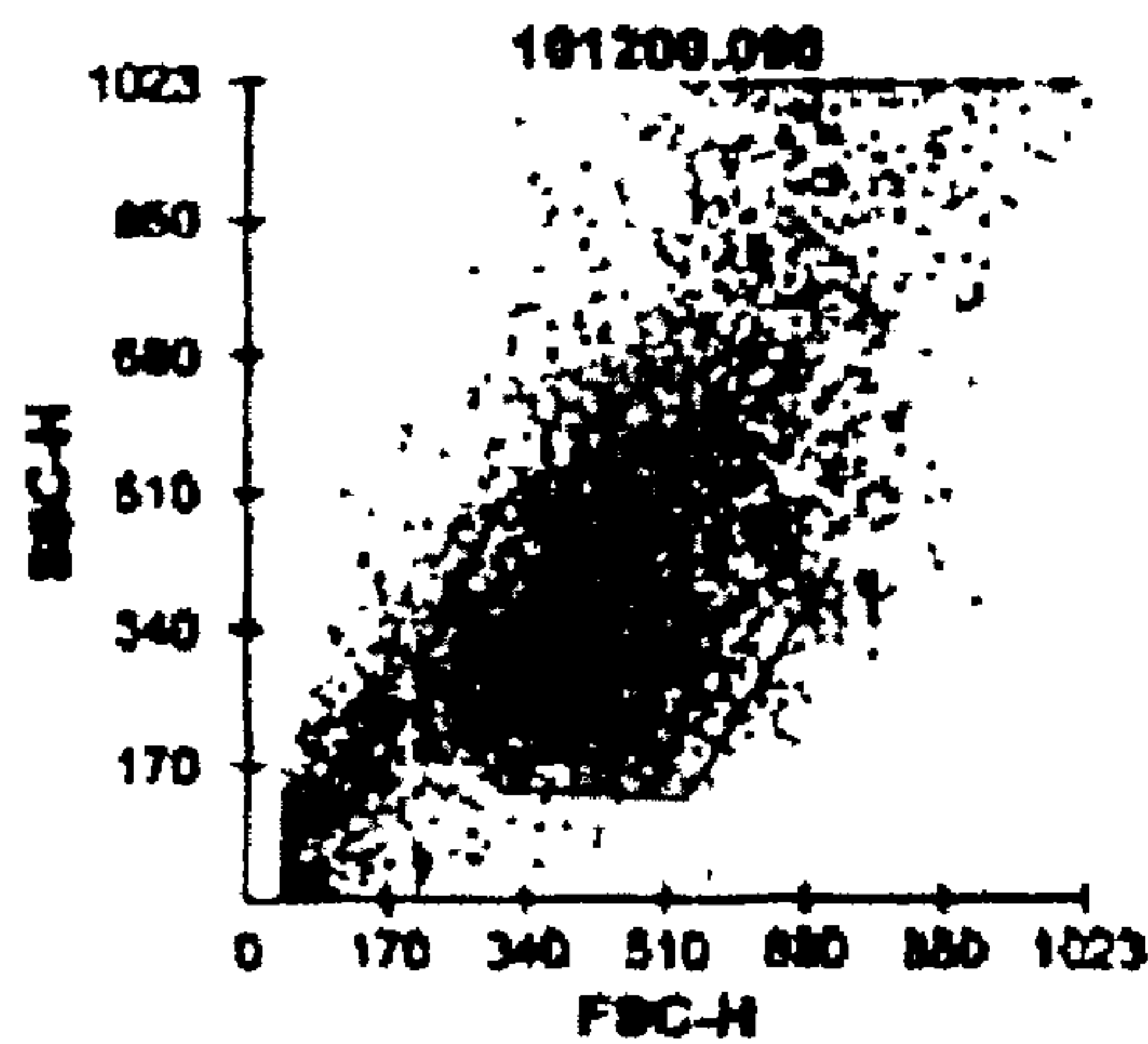
D: 250 ng human IgE-anti NP + 250ng PS IgE

Figure 9

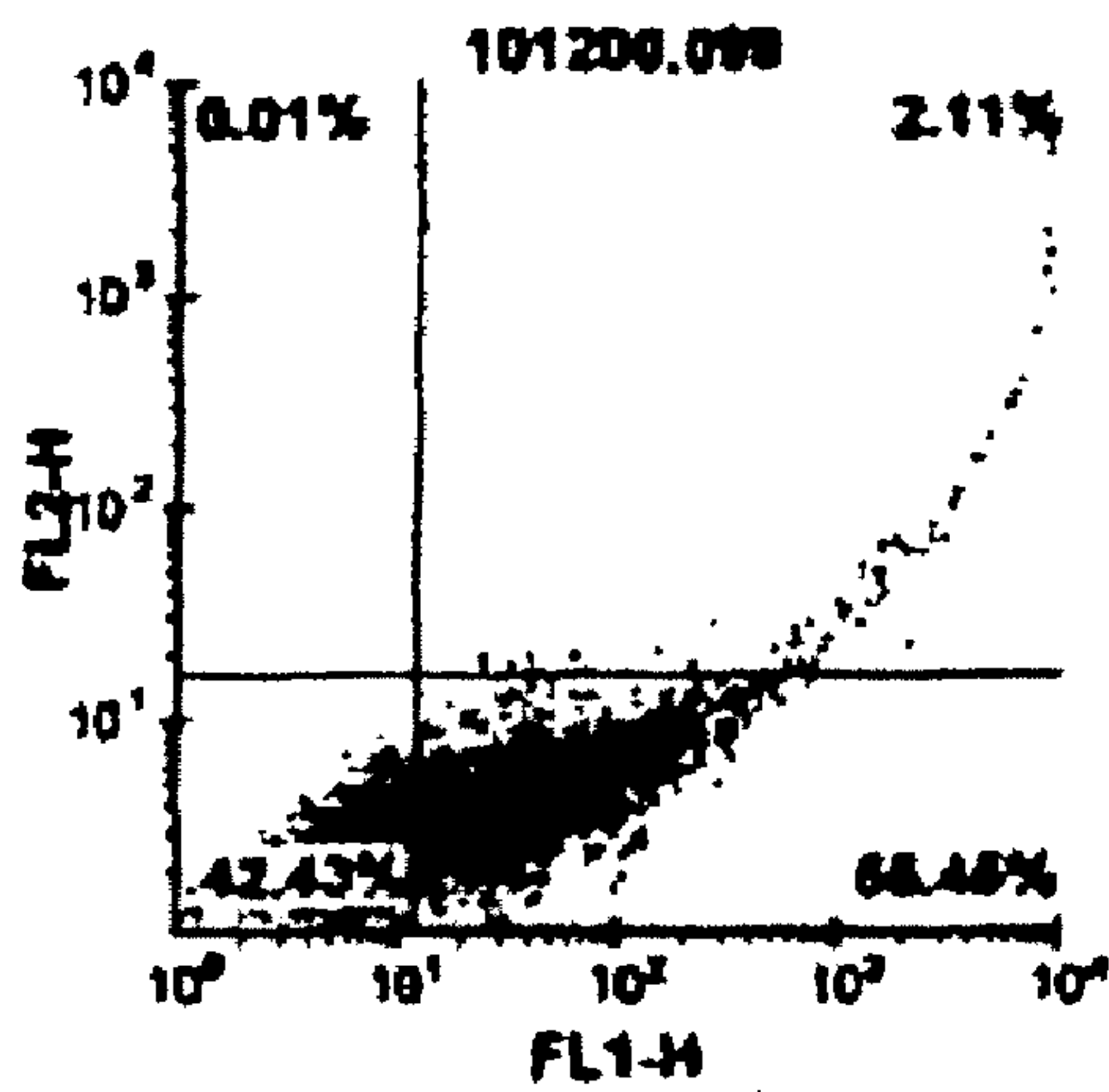
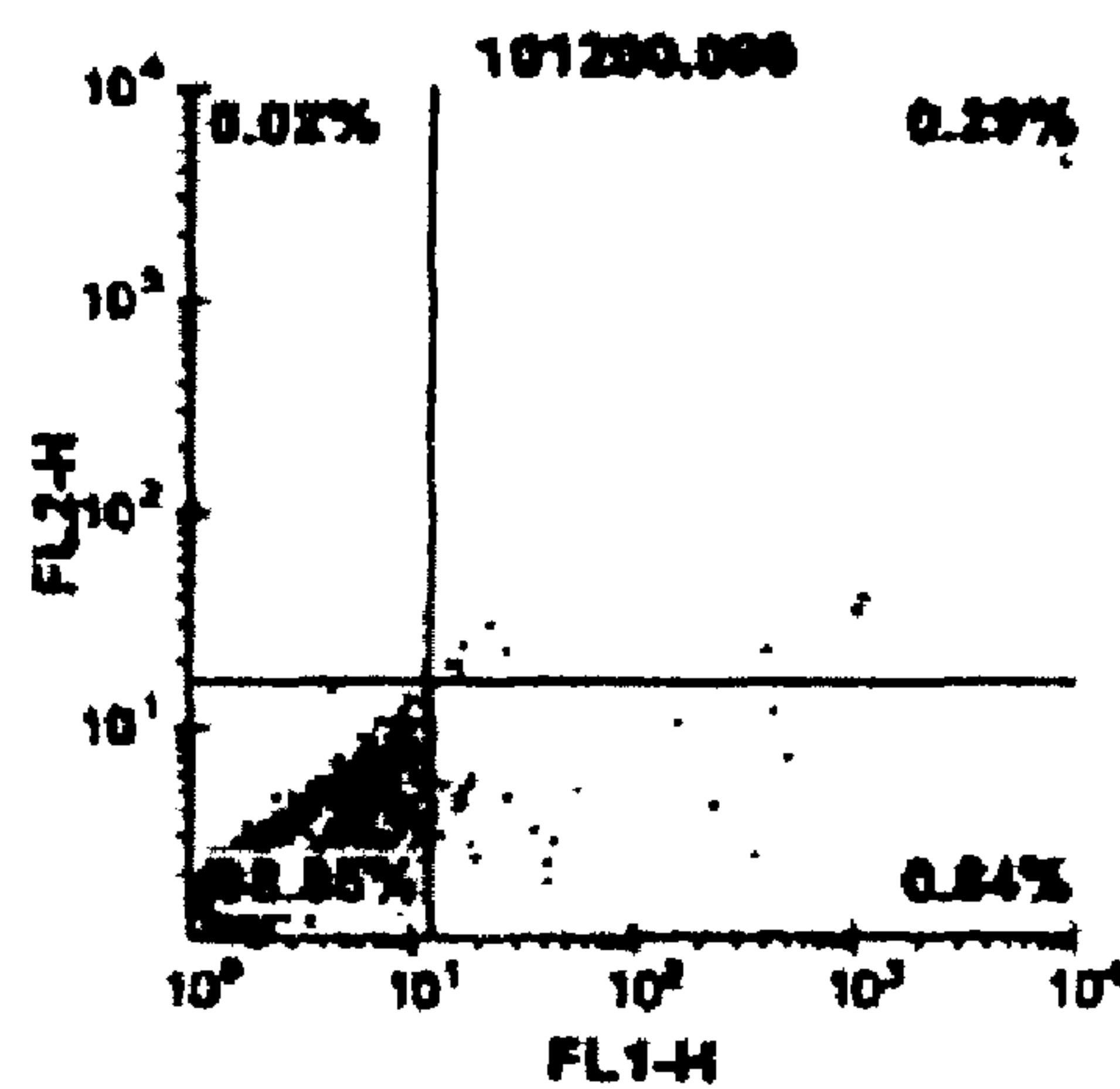
FIGURE 10

GE2 binding to HMC-1 cells that express FcγRIIb but not FcεRIa

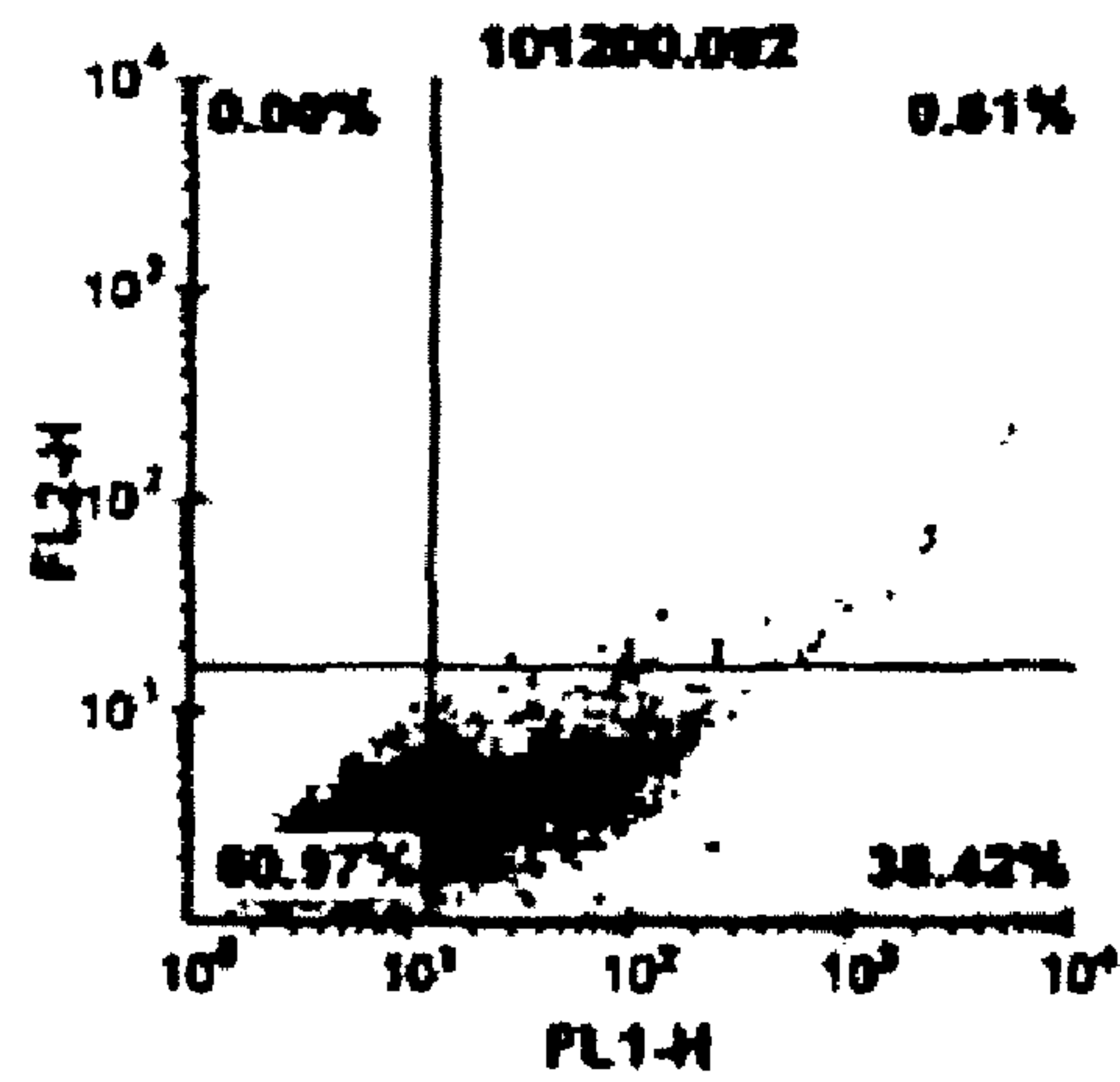
A. Cell gating



B. Control staining with goat anti-human IgG



C. Human IgG followed by staining with goat anti-human IgG

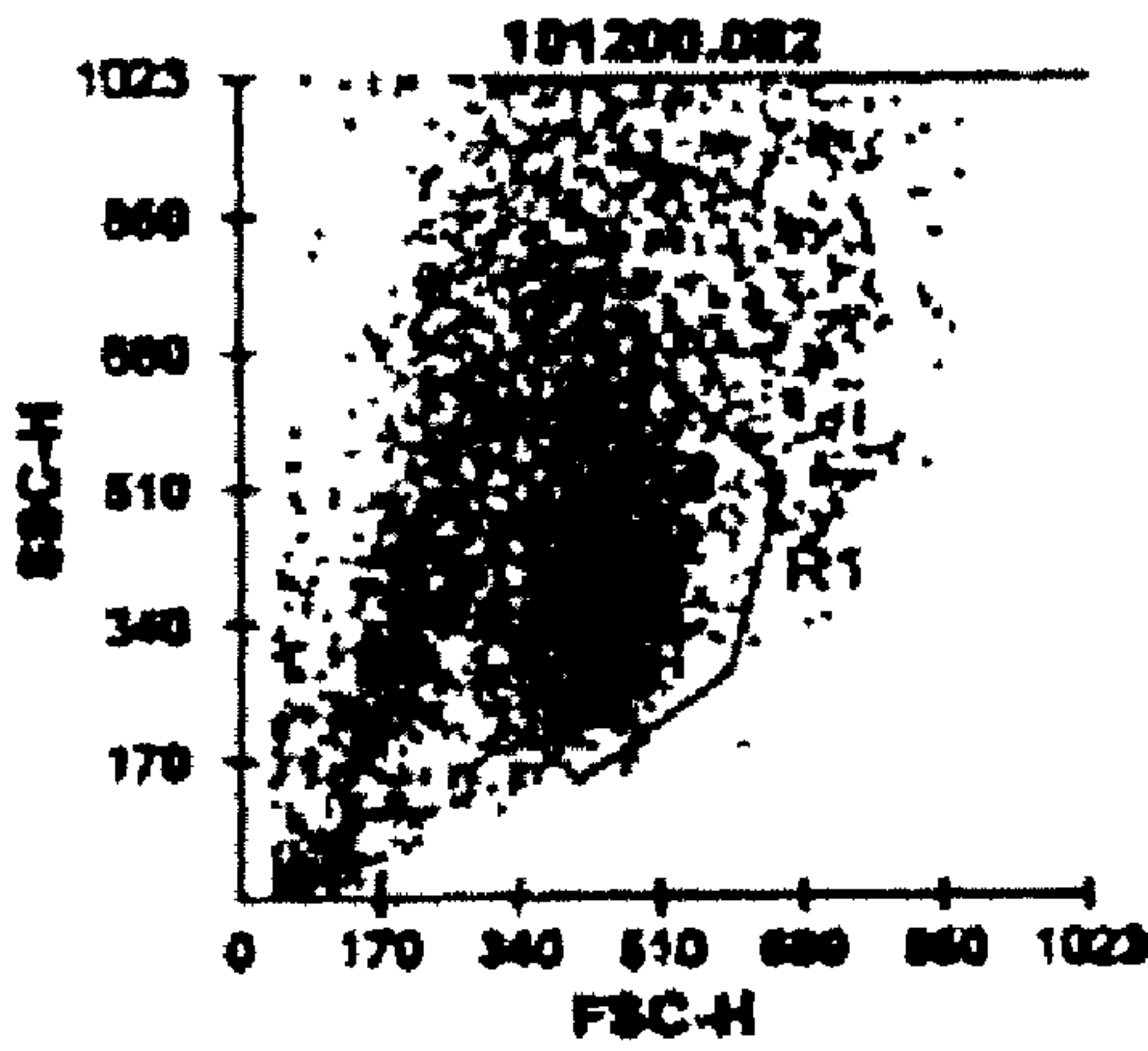


D. GE2 protein followed by staining with goat anti-human IgG

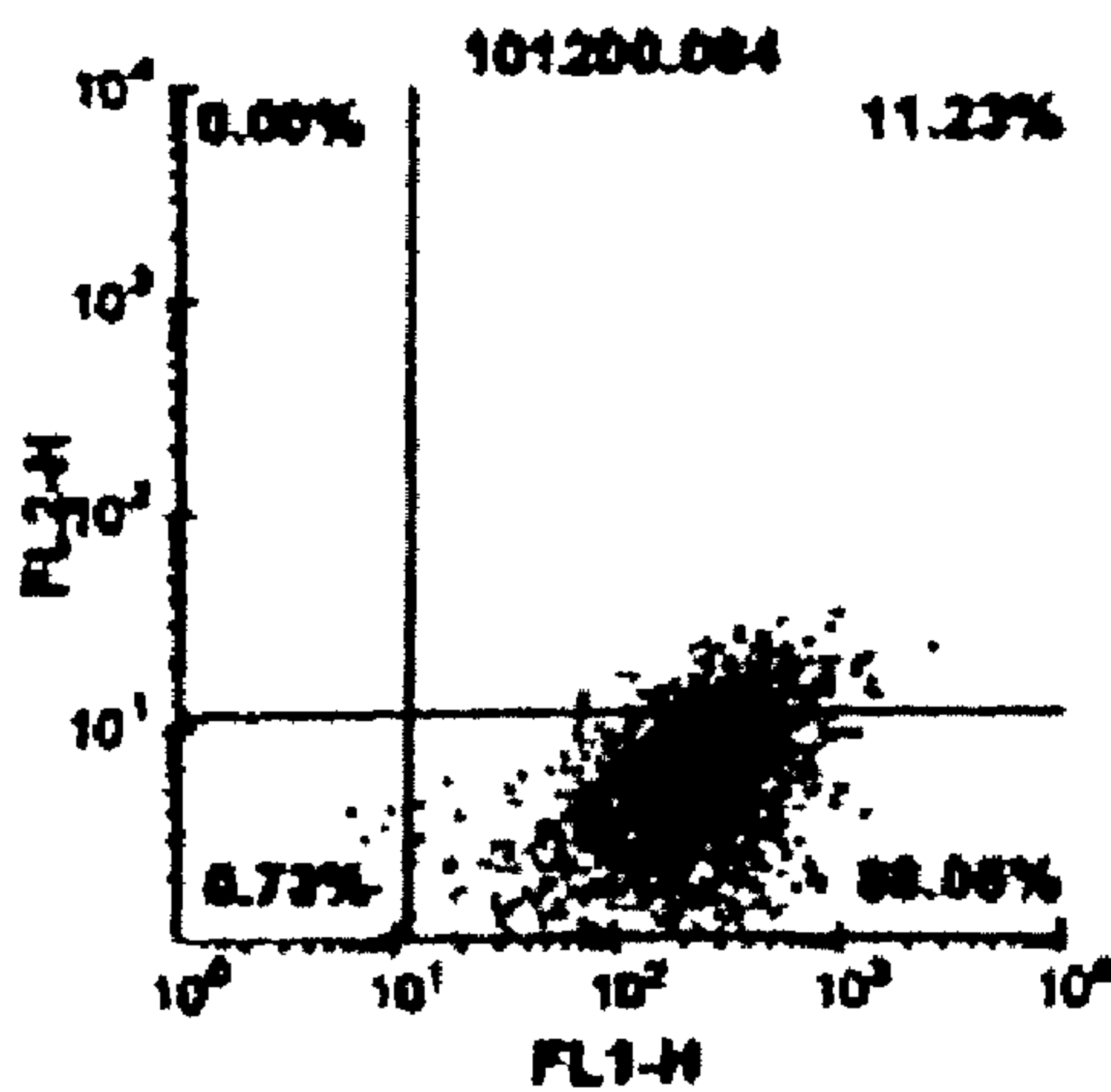
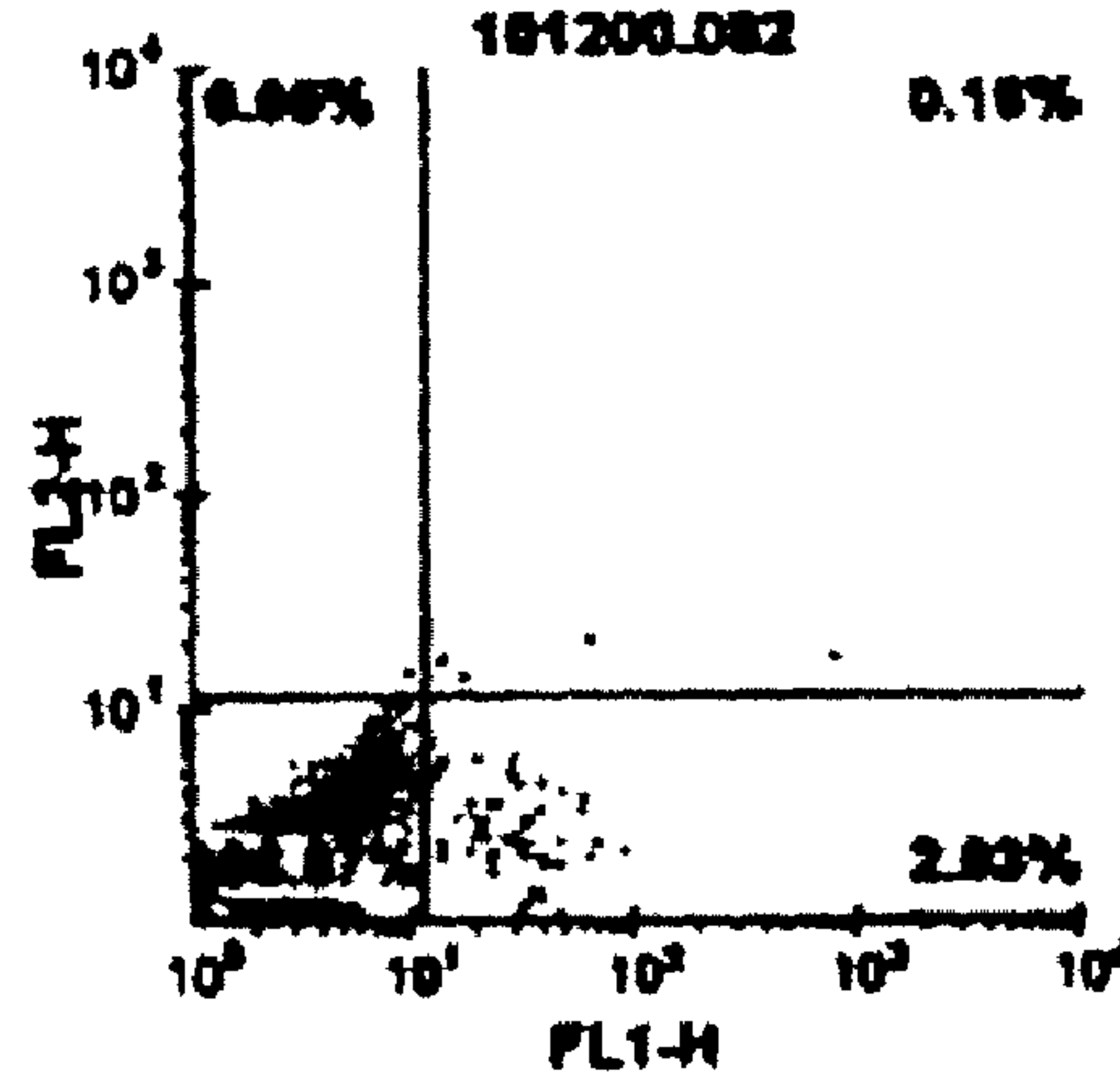
FIGURE 11

GE2 binding to 3D10 cells that express FcεRIa but not FcγRIIb

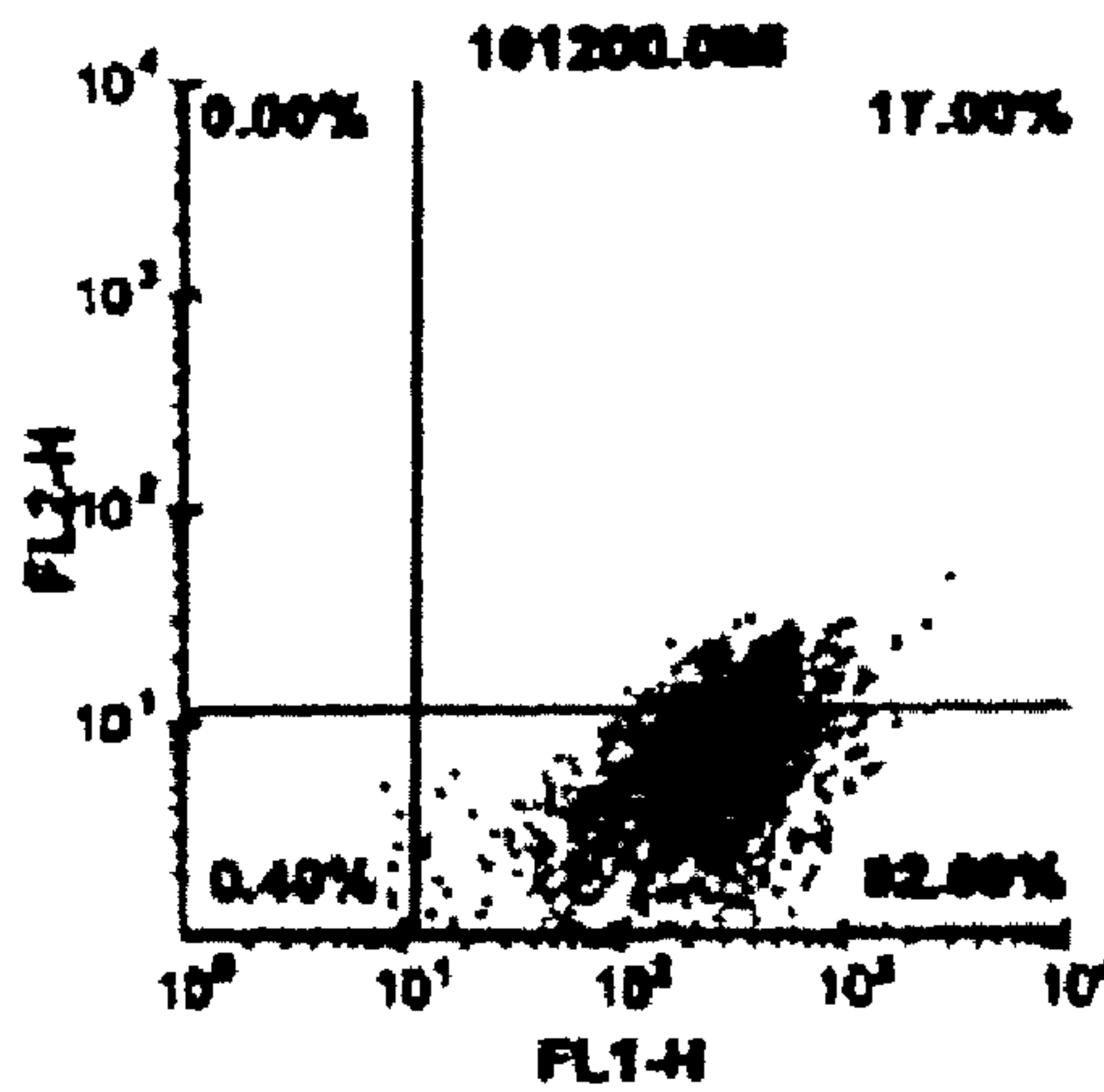
A. Cell gating on 3D10 cells which express FcεRIa but not FcγR



B. Staining with goat anti-human IgE alone



C. Human IgE myeloma followed by staining with goat anti-human IgE



D. GE2 followed by staining with goat anti-human IgE

FUSION MOLECULES AND TREATMENT OF IGE-MEDIATED ALLERGIC DISEASES

RELATED APPLICATIONS

This application is a continuation of, and claims priority under 35 USC §120 to, U.S. application Ser. No. 09/847,208 filed May 1, 2001 now U.S. Pat. No. 7,265,208, the entire disclosure which is hereby incorporated by reference.

This invention was made with Government support under Grant No. AI15251, awarded by the National Institutes of Health. The Government has certain rights in this invention.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The invention concerns a new approach for the management of IgE-mediated allergic diseases and other disorders mediated through IgE receptors (FcεRs) using novel fusion molecules that are able to complex with an FcεR and an inhibitory receptor expressed on mast cells, basophils, or B cells, including inhibitory receptors having an immune receptor tyrosine-based inhibitory (ITIM) motif.

2. Description of the Related Art

Immunoglobulin receptors (also referred to as Fc receptors) are cell-surface receptors binding the constant region of immunoglobulins, and mediate various immunoglobulin functions other than antigen binding.

Fc receptors for IgE molecules are found on many cell types of the immune system (Fridman, W., *FASEB J.*, 5(12): 2684-90 (1991)). There are two different receptors currently known for IgE. IgE mediates its biological responses as an antibody through the multichain high-affinity receptor, FcεRI, and the low-affinity receptor, FcεRII. The high-affinity FcεRI, expressed on the surface of mast cells, basophils, and Langerhans cells, belongs to the immunoglobulin gene superfamily, and has a tetrameric structure composed of an α-chain, a β-chain and two disulfide-linked γ-chains (Adamczewski, M., and Kinet, J. P., *Chemical Immunol.*, 59:173-190 (1994)) that are required for receptor expression and signal transduction (Tunon de Lara, *Rev. Mal. Respir.*, 13(1):27-36 (1996)). The α-chain of the receptor interacts with the distal portion of the third constant domain of the IgE heavy chain. The specific amino acids of human IgE involved in binding to human FcεRI have been identified as including Arg-408, Ser-411, Lys-415, Glu-452, Arg-465, and Met-469 (Presta et al., *J. Biol. Chem.* 269:26368-73 (1994)). The interaction is highly specific with a binding constant of about $10^{10}M^{-1}$.

The low-affinity FcεRII receptor, represented on the surface of inflammatory cells, including eosinophils, leukocytes, B lymphocytes, and platelets, did not evolve from the immunoglobulin superfamily but has substantial homology with several animal lectins (Yodoi et al., *Ciba Found. Symp.*, 147: 133-148 (1989)) and is made up of a transmembrane chain with an intracytoplasmic NH₂ terminus. The low-affinity receptor, FcεRII (CD23) is currently known to have two forms (FcεRIIa and FcεRIIb), both of which have been cloned and sequenced. They differ only in the N-terminal cytoplasmic region, the extracellular domains being identical. FcεRIIa is normally expressed on B cells, while FcεRIIb is expressed on T cells, B cells, monocytes and eosinophils upon induction by the cytokine IL-4.

Through the high-affinity IgE receptor, FcεRI, IgE plays key roles in an array of acute and chronic allergic reactions, including asthma, allergic rhinitis, atopic dermatitis, severe food allergies, chronic urticaria and angioedema, as well as the serious physiological condition of anaphylactic shock as

results, for example, from bee stings or penicillin allergy. Binding of a multivalent antigen (allergen) to antigen specifically bound to FcεRI on the surface of mast cells and basophils stimulates a complex series of signaling events that culminate in the release of host vasoactive and proinflammatory mediators contributing to both acute and late-phase allergic responses (Metcalf et al. *Physiol. Rev.* 77:1033-1079 (1997)).

The function of the low affinity IgE receptor, FcεRII (also referred to as CD23), found on the surface of B lymphocytes, is much less well established than that of FcεRI. FcεRII, in a polymeric state, binds IgE, and this binding may play a role in controlling the type (class) of antibody produced by B cells.

Three groups of receptors that bind the constant region of human IgG have so far been identified on cell surfaces: FcγRI (CD64), FcγRII (CD32), and FcγRIII (CD16), all of which belong to the immunoglobulin gene superfamily. The three Fcγ receptors have a large number of various isoforms.

Along with the stimulatory FcεRI, mast cells and basophils co-express an immunoreceptor tyrosine-based inhibition motif (ITIM)-containing inhibitory low-affinity receptor, FcγRIIb, that acts as a negative regulator of antibody function. FcγRIIb represents a growing family of structurally and functionally similar inhibitory receptors, the inhibitory receptor superfamily (IRS), that negatively regulate ITAM-containing immune receptors (Ott and Cambier, *J. Allergy Clin. Immunol.*, 106:429-440 (2000)) and a diverse array of cellular responses. Coaggregation of an IRS member with an activating receptor leads to phosphorylation of the characteristic ITIM tyrosine and subsequent recruitment of the SH2 domain-containing protein tyrosine phosphatases, SHP-1 and SHP-2, and the SH2 domain-containing phospholipases, SHIP and SHIP2 (Cambier, J. C., *Proc. Natl. Acad. Sci. USA*, 94:5993-5995 (1997)). Possible outcomes of the coaggregation include inhibition of cellular activation, as demonstrated by the coaggregation of FcγRIIb and B-cell receptors, T-cell receptors, activating receptors, including FcεRI, or cytokine receptors (Malbec et al., *Curr. Top. Microbiol. Immunol.*, 244:13-27 (1999)).

Most studies have so far concentrated on elucidating the mechanisms of FcγRII, in particular FcγRIIb, function. The three alternatively spliced isoforms of the FcγRIIb receptor, of which FcγRIIb1' is only found in mice, and FcγRIIb1 and FcγRIIb2 are expressed in both humans and mice, have Ig-like loops and a conserved ITIM, but differ in their cytoplasmic domains. Co-crosslinking of the high-affinity FcεRI receptor and the inhibitory low-affinity receptor FcγRII blocks a number of processes, including FcεRI-mediated secretion, IL-4 production, Ca²⁺ mobilization, Syk phosphorylation, and FcεRI-mediated basophil and mast cell activation. In B cells, co-crosslinking of the B-cell receptor and FcγRIIb inhibits B-cell receptor-mediated cell activation (Cambier, J. C., *Proc. Natl. Acad. Sci.*, 94:5993-5995 (1997); Daeron, M., *Annu. Rev. Immunol.*, 5:203-234 (1997)), and specifically, inhibits B-cell receptor-induced blastogenesis and proliferation (Chan et al., *Immunology*, 21:967-981 (1971); Phillips and Parker, *J. Immunol.*, 132:627-632 (1984)) and stimulates apoptosis (Ashman et al., *J. Immunol.*, 157:5-11 (1996)). Coaggregation of FcγRIIb1 or FcγRIIb2 with FcεRI in rat basophilic leukemia cells, inhibits FcεRI-mediated release of serotonin and TNF-α (Daeron et al., *J. Clin. Invest.*, 95:577-85 (1995); Daeron et al., *Immunity*, 3:635-646 (1995)).

Another ITIM-containing receptor expressed on mast cells that has been described to prevent IgE-mediated mast cell activation when coligated with FcεRI, is a 49 kDa glycoprotein member of the immunoglobulin superfamily, termed

gp49b1 (gp91) (see, e.g. Wagtmann et al., *Current Top. Microbiol. Immunol.* 244:107-113 (1999); Katz, H. R., *Int. Arch Allergy Immunol.* 118:177-179 (1999); and Lu-Kuo et al., *J. Biol. Chem.* 274:5791-96 (1999)). Gp49b1 was originally identified in mice, while human counterparts of the gp49 family, including gp49b1, have been cloned by Arm et al., *J. Immunol.* 15:2342-2349 (1997). Further ITIM-containing receptors, several expressed in mast cells, basophils or B cells are reviewed by Sinclair N R, *Scand. J. Immunol.* 50:10-13 (1999).

Despite advances in understanding the cellular and molecular mechanisms that control allergic responses and improved therapies, the incidence of allergic diseases, especially asthma, has increased dramatically in recent years in both developed and developing countries (Beasley et al., *J. Allergy Clin. Immunol.* 105:466-472 (2000); Peat and Li, *J. Allergy Clin. Immunol.* 103:1-10 (1999)). Allergic diseases can be treated, for example, by allergen-based vaccination, in which increasing doses of allergen are given by injection over years. This approach is costly, time consuming, poorly or not efficacious in many allergic conditions, and has serious side-effects, including death in some instances. Mild asthma can usually be controlled in most patients by relatively low doses of inhaled corticosteroids, while moderate asthma is usually managed by the additional administration of inhaled long-acting β -antagonists or leukotriene inhibitors. The treatment of severe asthma is still a serious medical problem. In addition, many of the therapeutics currently used in allergy treatment have serious side-effects. Although an anti-IgE antibody currently in clinical trials (rhuMAb-E25, Genentech, Inc.) and other experimental therapies (e.g. antagonists of IL-4) show promising results, there is need for the development of additional therapeutic strategies and agents to control allergic disease, such as asthma, severe food allergy, and chronic urticaria and angioedema.

The object of this invention is to provide a novel therapeutic strategy designed to cross-link inhibitory receptors expressed on mast cells, basophils and/or B cells, such as an ITIM-containing Fc γ RIIb or gp49b1 receptor, or p91/PIR-B receptor, with Fc ϵ RI or Fc ϵ RII, for the treatment of conditions associated with anaphylactic hypersensitivity and atopic allergies, such as, for example, asthma, allergic rhinitis, atopic dermatitis, severe food allergies, some forms of chronic urticaria and angioedema, as well as the serious physiological condition of anaphylactic shock as results, for example, from bee stings or penicillin allergy.

SUMMARY OF THE INVENTION

The present invention provides novel bi-functional compounds that co-crosslink inhibitory receptors with Fc ϵ receptors and block Fc ϵ receptor-mediated biological activities, as well as methods of making and using such compounds, and compositions and articles of manufacture comprising them.

In one aspect the invention concerns an isolated fusion molecule comprising a first polypeptide sequence capable of specific binding, to a native inhibitory receptor comprising an immune receptor tyrosine-based inhibitory motif (ITIM), expressed on mast cells, basophils and/or B cells, functionally connected to a second polypeptide sequence capable of specific binding, directly or indirectly, to a native IgE receptor (Fc ϵ R). Preferably, the inhibitory receptor is a type I transmembrane molecule with an Ig-like domain, such as, for example, a low-affinity IgG receptor Fc γ RIIb, an inhibitory receptor of the gp49 family, e.g. gp49b1, p91/PIR-B, leukocyte-associated immunoglobulin-like receptor-1 (LAIR-1), LIR-1, or CD22.

The IgE receptor may be a high-affinity Fc ϵ RI receptor, or a low-affinity Fc ϵ RII receptor (CD23).

More preferably, the inhibitory receptor is a low-affinity Fc γ RIIb receptor, most preferably native human Fc γ RIIb, and the IgE receptor is a high-affinity Fc ϵ RI receptor, most preferably native human Fc ϵ RI, although fusion molecules including sequences capable of specific binding, directly or indirectly, to the low-affinity IgE receptor Fc ϵ RII are also within the scope of the invention.

In a particularly preferred embodiment, the two receptors are both of human origin, and the first and second polypeptide sequences present in the fusion molecules are human IgG, e.g. IgG₁, and IgE heavy chain constant region sequences, respectively.

In a preferred embodiment, the second polypeptide sequence comprises a sequence of an allergen protein, which is capable of indirect binding to a high- or low-affinity IgE receptor via an allergen-specific IgE molecule. In this embodiment, the second polypeptide sequence may comprise part or whole of a native or variant allergen protein, such as a food or pollen allergen.

The first and second polypeptide sequences may be connected via a linker, e.g. a polypeptide linker or a non-polypeptide bifunctional linker, or may be directly fused to each other. The length of the polypeptide linker typically is about 5 to 25 amino acid residues, preferably about 10 to 25 amino acid residues, most preferably about 15 to 25 amino acid residues.

In a particular embodiment, the first polypeptide sequence in the fusion molecule retains the residues from a native IgG heavy chain constant region that are required to bind to the targeted IgG inhibitory receptor, e.g. Fc γ RIIb. Similarly, in a particular embodiment, the second polypeptide sequence in the fusion molecule retains the residues from a native IgE heavy chain constant region that are required for binding to the targeted IgE receptor, such as Fc ϵ RI or Fc ϵ RII.

In another embodiment, the first polypeptide sequence comprises an amino acid sequence having at least about 80%, preferably at least about 85%, more preferably at least about 90%, even more preferably at least about 95%, most preferably at least about 99% sequence identity with the hinge-CH2-CH3 portion of a native IgG immunoglobulin heavy chain constant region. The IgG preferably is, but does not need to be, IgG₁. Indeed, the IgG portion of the molecule can derive from the heavy chain constant region of any IgG subclass, including IgG₁, IgG₂, IgG₃ and IgG₄.

In yet another embodiment, the first polypeptide sequence comprises an amino acid sequence having at least about 80%, preferably at least about 85%, more preferably at least about 90%, even more preferably at least about 95%, most preferably at least about 99% sequence identity with the receptor-binding domain of a ligand of another native ITIM-containing inhibitory receptor expressed on mast cells, basophils, or B cells, such as, without limitation, a native gp49b1, p91/PIR-B, LAIR-1, LIR-1, or CD11 receptor.

In another particular embodiment, the second polypeptide sequence in the fusion molecule comprises an amino acid sequence having at least about 80%, preferably at least about 85%, more preferably at least about 90%, even more preferably at least about 95%, most preferably at least about 99% sequence identity with the CH2-CH3-CH4 portion of a native IgE immunoglobulin heavy chain constant region.

In yet another embodiment, the second polypeptide sequence in the fusion molecule comprises an amino acid sequence having at least about 80%, preferably at least about 85%, more preferably at least about 90%, even more prefer-

ably at least about 95%, most preferably at least about 99% sequence identity with a native allergen protein or a fragment thereof.

In a further embodiment, the first polypeptide sequence in the fusion molecule comprises an amino acid sequence encoded by nucleic acid hybridizing under stringent conditions to the complement of the coding sequence of the hinge-CH2-CH3 portion of a native IgG immunoglobulin heavy chain constant region, and retains the ability to bind an IgG inhibitory receptor, preferably human Fc γ RIIb. The IgG preferably is, but does not need to be, IgG₁.

In a still further preferred embodiment, the second polypeptide sequence in the fusion molecule comprises an amino acid sequence encoded by nucleic acid hybridizing under stringent conditions to the complement of the coding sequence of the CH2-CH3-CH4 portion of a native IgE immunoglobulin heavy chain constant region, and retains the ability to bind a high-affinity IgE receptor, preferably human Fc ϵ RI.

In yet another embodiment, the second polypeptide sequence in the fusion molecule comprises an amino acid sequence encoded by nucleic acid hybridizing under stringent conditions to the complement of the coding sequence of all or part of a native allergen protein.

A particularly preferred molecule of the invention comprises the hinge-CH2-CH3 portion of an IgG, such as IgG₁, immunoglobulin heavy chain constant region functionally linked to the CH2-CH3-CH4 portion of an IgE immunoglobulin heavy chain constant region via a 15 amino acids polypeptide linker. In a preferred embodiment, the IgG₁ hinge-CH2-CH3 sequence is connected at its C-terminus to the N-terminus of the IgE CH2-CH3-CH4 sequence via the 15 amino acids polypeptide linker. Preferably both immunoglobulin heavy chain sequences are of human origin.

In another aspect, the invention concerns isolated nucleic acid molecules encoding polypeptide fusions of the present invention. The invention also concerns vectors comprising such nucleic acid molecules, and recombinant host cells transformed with such vectors.

In a further aspect, the invention concerns a pharmaceutical composition comprising a fusion molecule as hereinabove defined in admixture with a pharmaceutically acceptable ingredient. The pharmaceutical composition is preferably used for the treatment of an IgE-mediated response, such as an acute or late phase allergic reaction, including, without limitation, immediate hypersensitivity reactions. In a preferred embodiment, the pharmaceutical composition is for the treatment of a condition associated with anaphylactic hypersensitivity or an atopic allergy, such as asthma, allergic rhinitis, atopic dermatitis, severe food allergies, chronic urticaria, angioedema, and/or anaphylactic shock.

In a still further aspect, the invention concerns an article of manufacture comprising a container, a fusion molecule as hereinabove defined within the container, and a label or package insert on or associated with the container. The label or package insert preferably comprises instructions for the treatment of a condition associated with an IgE-mediated biological response, such as a condition associated with anaphylactic hypersensitivity or an atopic allergy, e.g. asthma, allergic rhinitis, atopic dermatitis, severe food allergies, chronic urticaria, angioedema, and/or anaphylactic shock.

In yet another aspect, the invention concerns a method for the treatment of a condition associated with an IgE-mediated biological response, comprising administering an effective amount of a fusion molecule as hereinabove defined to a subject in need. The subject preferably is a human patient, and the condition to be treated (including prevention), preferably

is asthma, allergic rhinitis, atopic dermatitis, severe food allergies, chronic urticaria, angioedema, and/or anaphylactic shock.

In addition to the aspects discussed above, the present invention also contemplates fusion molecules suitable for coaggregation of other inhibitory receptors with IgE receptors, such as Fc ϵ RI or Fc ϵ R2. For example, a fusion molecule comprising a c-kit ligand sequence, capable of specific binding the receptor PTK c-Kit, fused to a polypeptide sequence capable of specific binding, directly or indirectly, to an IgE receptor, such as Fc ϵ RI or Fc ϵ R2, is also contemplated. Such fusion molecules are expected to negatively regulate the expression of mast cells, and find utility in the treatment of conditions associated with anaphylactic hypersensitivity and atopic allergies.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 shows the nucleotide sequence encoding the human IgG₁ heavy chain constant region (SEQ ID NO: 1).

FIG. 2 shows the amino acid sequence of the human IgG₁ heavy chain constant region (SEQ ID NO: 2). In the sequence, the CH1 domain extends from amino acid position 122 to amino acid position 219, the hinge region extends from amino acid position 220 to amino acid position 231, the CH2 domain extends from amino acid position 232 to amino acid position 344, and the CH3 domain extends from amino acid position 345 to amino acid 451 (the C-terminus).

FIG. 3 shows the amino acid sequence of the hinge-CH2-CH3 portion of the human IgG₁ heavy chain constant region (SEQ ID NO: 3).

FIG. 4 shows the nucleotide sequence encoding the human IgE heavy chain constant region (SEQ ID NO: 4).

FIG. 5 shows the amino acid sequence of the human IgE heavy chain constant region (SEQ ID NO: 5).

FIG. 6 shows the amino acid sequence of the CH2-CH3-CH4 portion of the human IgE heavy chain constant region (SEQ ID NO: 6).

FIG. 7 shows the amino acid sequence of the γ hinge-CH₂-CH₃-(Gly₄Ser)₃-CH₂-CH₃-CH₃ fusion molecule (GE2) of the invention (SEQ ID NO: 7).

FIG. 8 illustrates the dose-dependent inhibition of basophil histamine release using the fusion protein GE2 (\pm SEM; n=3 separate donors, each in duplicate). Purified human blood basophils were acid stripped and then sensitized with humanized anti-NP IgE, labeled as IgE, alone or in the presence of GE2 protein or PS that is a purified human IgE myeloma protein. One hour later, cells were challenged with NP-BSA and the resulting level of histamine release measured.

FIG. 9 shows results obtained in the transgenic passive cutaneous anaphylaxis (PCA) model described in the Example. Sites were injected with 250 ng of human anti-IgE NP along with the indicated amounts of PS (non-specific human IgE) or GE2 chimeric fusion protein. Four hours later, the animals were challenged intravenously (IV) with 500 μ g of NP-BSA.

FIG. 10 illustrates GE2 binding to HMC-1 cells that express Fc γ RIIb but not Fc ϵ RIa.

FIG. 11 illustrates GE2 binding to 3D10 cells that express Fc ϵ RIa but not Fc γ RIIb.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

I. Definitions

Unless defined otherwise, technical and scientific terms used herein have the same meaning as commonly understood

by one of ordinary skill in the art to which this invention belongs. One skilled in the art will recognize many methods and materials similar or equivalent to those described herein, which could be used in the practice of the present invention. Indeed, the present invention is in no way limited to the methods and materials described. For purposes of the present invention, the following terms are defined below.

The term “functionally connected” with reference to the first and second polypeptide sequences included in the fusion molecules herein, is used to indicate that such first and second polypeptide sequences retain the ability to bind to the respective receptors. Thus, after being connected to a second polypeptide sequence, the first polypeptide sequence retains the ability of specific binding to a native IgG inhibitory receptor, such as a low-affinity FcγRIIb receptor. Similarly, after being connected to a first polypeptide sequence, the second polypeptide sequence retains the ability of specific binding, directly or indirectly, i.e. through a third polypeptide sequence, to a native IgE receptor, such as a native high-affinity IgE receptor, e.g. native human FcεRI, or a native low-affinity IgE receptor, e.g. FcεRII. As a result, the fusion molecule, comprising the first and second polypeptide sequences functionally connected to each other, is capable of cross-linking the respective native receptors, such as, for example, FcγRIIb and FcεRI or FcεRII. In order to achieve a functional connection between the two binding sequences within the fusion molecules of the invention, it is preferred that they retain the ability to bind to the corresponding receptor with a binding affinity similar to that of a native immunoglobulin heavy chain or other native polypeptide binding to that receptor.

The binding is “specific” when the binding affinity of a molecule for a binding target, e.g. an IgG or IgE receptor, is significantly higher (preferably at least about 2-times, more preferably at least about 4-times, most preferably at least about 6-times higher) than the binding affinity of that molecule to any other known native polypeptide. Since you do not define how one determines the universe of “other known native polypeptide(s)”, this definition could be considered indefinite. What about defining specific binding as preferential binding in the presence of a competitor (you could even name possible competitors).

The term “inhibitory receptor” is used in the broadest sense and refers to a receptor capable of down-regulating a biological response mediated by another receptor, regardless of the mechanism by which the down-regulation occurs.

The terms “receptor comprising an immune receptor tyrosine-based inhibitory motif (ITIM)” and “ITIM-containing receptor” is used to refer to a receptor containing one or more immune receptor tyrosine-based inhibitory motifs, ITIMs. The ITIM motif can be generally represented by the formula Val/Ile-Xaa-PTyr-Xaa-Xaa-Leu/Val (where Xaa represents any amino acid). ITIM-containing receptors include, without limitation, FcγRIIb, gp49b1/gp91 (Arm et al., *J. Biol. Chem.* 266:15966-73 (1991)), p91/PIR-B (Hayami et al., *J. Biol. Chem.* 272:7320-7 (1997)), LIR1-3, 5, 8, LAIR-1; CD22 (van Rossenberg et al., *J. Biol. Chem.* Jan. 4, 2001); CTL-4, CD5, p58/70/140 KIR, PIRB2-5; NKB1, Ly49 A/C/E/F/G, NKG2-A/B, APC-R, CD66, CD72, PD-1, SHPS-1, SIRP-α1, IL T1-5, MIR7, 10, hMIR(HM18), hMIR(HM9), Fas (CD95), TGFβ-R, TNF-R1, IFN-γ-R (α- and β-chains), mast cell function Ag, H2-M, HLA-DM, CD1, CD1-d, CD46, c-cbl, Pyk2/FADK2, P130 Ca rel prot, PGDF-R, LIF, LIR-R, CIS, SOCS13 and 3, as reviewed in Sinclair N R et al., supra. Ligands for many of these receptors are also known, such as, e.g. the ligand for CD95 is called CD95 ligand, the ligands for CTLA-4 are CD80 and CD86, the ligands of IFN-γ receptor is

IFN-γ, etc. Ligands for CD22 comprise the basic binding motif Nau5Ac-a(2,6)-Lac, and are discussed, for example in van Rossenberg et al., 2001, supra.

The term “IgG inhibitory receptor” is used to define a member of the inhibitory receptor superfamily (IRS), now know or hereinafter discovered, that is capable of attenuating an FcεR-mediated response, regardless of whether it is mediated via IgE acting through a high-affinity IgE receptor, e.g. FcεRI, or a low-affinity IgE receptor, or by another mechanism such as an autoantibody to the FcεR. The response preferably is an IgE-mediated allergic response, such as a type I (immediate hypersensitivity) reaction but could include autoimmune reactions due to anti-FcεRI α-chain antibodies that have been reported in about half of the cases of chronic idiopathic urticaria.

The term “native” or “native sequence” refers to a polypeptide having the same amino acid sequence as a polypeptide that occurs in nature. A polypeptide is considered to be “native” in accordance with the present invention regardless of its mode of preparation. Thus, such native sequence polypeptide can be isolated from nature or can be produced by recombinant and/or synthetic means. The terms “native” and “native sequence” specifically encompass naturally-occurring truncated or secreted forms (e.g., an extracellular domain sequence), naturally-occurring variant forms (e.g., alternatively spliced forms) and naturally-occurring allelic variants of a polypeptide.

The terms “native FcγRIIb,” “native sequence FcγRIIb,” “native low-affinity IgG inhibitory receptor FcγRIIb,” and “native sequence low-affinity IgG inhibitory receptor FcγRIIb” are used interchangeably, and refer to FcγRIIb receptors of any species, including any mammalian species, as occurring in nature. Preferably, the mammal is human. FcγRIIb is an isoform of the low-affinity IgG receptor FcγRII containing an immunoreceptor tyrosine-based inhibition motif (ITIM). This receptor is the principal FcγRII species in human peripheral blood basophils and cord blood-derived mast cells. For further details see, for example, Malbec and Fridman, *Curr. Top. Microbiol. Immunol.* 244:13-27 (1999); Cambier, J. C., *Proc. Natl. Acad. Sci. USA* 94:5993-5995 (1997); and Ott and Cambier, *J. Allergy Clin. Immunol.* 106 (3):429-440 (2000). FcγRIIb has three alternatively spliced forms designated FcγRIIb1, FcγRIIb1', and FcγRIIb2, which differ only in their cytoplasmic domain sequences. All three alternatively spliced isoforms contain two extracellular Ig-like loops and a single conserved ITIM motif within their cytoplasmic tails, and are specifically included within the definition of FcγRIIb, along with other splice variants that might be identified in the future.

The terms “native FcεRI,” “native sequence FcεRI,” “native high-affinity IgE receptor FcεRI,” and “native sequence high-affinity IgE receptor FcεRI” are used interchangeably and refer to FcεRI receptors of any species, including any mammalian species, that occurs in nature. FcεRI is a member of the multi-subunit immune response receptor (MIRR) family of cell surface receptors that lack intrinsic enzymatic activity but transduce intracellular signals through association with cytoplasmic tyrosine kinases. For further details see, for example, Kinet, J. P., *Annu. Rev. Immunol.* 17:931-972 (1999) and Ott and Cambier, *J. Allergy Clin. Immunol.*, 106:429-440 (2000).

The terms “native FcεRII (CD23),” “native sequence FcεRII (CD23),” “native low-affinity IgE receptor FcεRII (CD23),” “native sequence low-affinity IgE receptor FcεRII (CD23)” are used interchangeably and refer to FcεRII (CD23) receptors of any species, including any mammalian species, that occur in nature. Several groups have cloned and

expressed low-affinity IgE receptors of various species. The cloning and expression of a human low-affinity IgE receptor is reported, for example, by Kikutani et al., *Cell* 47:657-665 (1986), and Ludin et al., *EMBO J.* 6:109-114 (1987). The cloning and expression of corresponding mouse receptors is disclosed, for example, by Gollnick et al., *J. Immunol.* 144:1974-82 (1990), and Kondo et al., *Int. Arch. Allergy Immunol.* 105:38-48 (1994). The molecular cloning and sequencing of CD23 for horse and cattle has been recently reported by Watson et al., *Vet. Immunol. Immunopathol.* 73:323-9 (2000). For an earlier review of the low-affinity IgE receptor see also Delespesse et al., *Immunol. Rev.* 125:77-97 (1992).

The term "mammal" or "mammalian species" refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, goats, rabbits, as well as rodents such as mice and rats, etc. Preferably, the mammal is human.

The term "polypeptide", in singular or plural, is used herein to refer to any peptide or protein comprising two or more amino acids joined to each other in a linear chain by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, and to longer chains, commonly referred to in the art as proteins. Polypeptides, as defined herein, may contain amino acids other than the 20 naturally occurring amino acids, and may include modified amino acids. The modification can be anywhere within the polypeptide molecule, such as, for example, at the terminal amino acids, and may be due to natural processes, such as processing and other post-translational modifications, or may result from chemical and/or enzymatic modification techniques which are well known to the art. The known modifications include, without limitation, acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cystine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. Such modifications are well known to those of skill and have been described in great detail in the scientific literature, such as, for instance, Creighton, T. E., *Proteins—Structure And Molecular Properties*, 2nd Ed., W.H. Freeman and Company, New York (1993); Wold, F., "Posttranslational Protein Modifications: Perspectives and Prospects," in *Posttranslational Covalent Modification of Proteins*, Johnson, B. C., ed., Academic Press, New York (1983), pp. 1-12; Seifter et al., "Analysis for protein modifications and nonprotein cofactors," *Meth. Enzymol.* 182:626-646 (1990), and Rattan et al., *Ann. N.Y. Acad. Sci.* 663:48-62 (1992).

Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. In fact, blockage of the amino or carboxyl group in a polypeptide, or both, by a covalent modification, is common in naturally occurring and synthetic polypeptides and such modifications may be present in polypeptides of the present invention, as well. For instance, the amino terminal residue of polypeptides made in *E. coli*, prior to proteolytic processing, almost invariably will

be N-formylmethionine. Accordingly, when glycosylation is desired, a polypeptide is expressed in a glycosylating host, generally eukaryotic host cells. Insect cells often carry out the same post-translational glycosylations as mammalian cells and, for this reason, insect cell expression systems have been developed to express efficiently mammalian proteins having native patterns of glycosylation.

It will be appreciated that polypeptides are not always entirely linear. For instance, polypeptides may be branched as a result of ubiquitination, and they may be circular, with or without branching, generally as a result of post-translational events, including natural processing and events brought about by human manipulation which do not occur naturally. Circular, branched and branched circular polypeptides may be synthesized by non-translation natural process and by entirely synthetic methods, as well. Such structures are within the scope of the polypeptides as defined herein.

Amino acids are represented by their common one- or three-letter codes, as is common practice in the art. Accordingly, the designations of the twenty naturally occurring amino acids are as follows: Alanine=Ala (A); Arginine=Arg (R); Aspartic Acid=Asp (D); Asparagine=Asn (N); Cysteine=Cys (C); Glutamic Acid=Glu (E); Glutamine=Gln (O); Glycine=Gly (G); Histidine=His (H); Isoleucine=Ile (I); Leucine=Leu (L); Lysine=Lys (K); Methionine=Met (M); Phenylalanine=Phe (F); Proline=Pro (P); Serine=Ser (S); Threonine=Thr (T); Tryptophan=Trp (W); Tyrosine=Tyr (Y); Valine=Val (V). The polypeptides herein may include all L-amino acids, all D-amino acids or a mixture thereof. The polypeptides comprised entirely of D-amino acids may be advantageous in that they are expected to be resistant to proteases naturally found within the human body, and may have longer half-lives.

The term "amino acid sequence variant" refers to molecules with some differences in their amino acid sequences as compared to a reference (e.g. native sequence) polypeptide. The amino acid alterations may be substitutions, insertions, deletions or any desired combinations of such changes in a native amino acid sequence.

Substitutional variants are those that have at least one amino acid residue in a native sequence removed and a different amino acid inserted in its place at the same position. The substitutions may be single, where only one amino acid in the molecule has been substituted, or they may be multiple, where two or more amino acids have been substituted in the same molecule.

Insertional variants are those with one or more amino acids inserted immediately adjacent to an amino acid at a particular position in a native amino acid sequence. Immediately adjacent to an amino acid means connected to either the α -carboxy or α -amino functional group of the amino acid.

Deletional variants are those with one or more amino acids in the native amino acid sequence removed. Ordinarily, deletional variants will have at least one amino acid deleted in a particular region of the molecule.

"Sequence identity" is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in a reference polypeptide sequence (e.g., a native polypeptide sequence), after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. The % sequence identity values are generated by the NCBI BLAST2.0 software as defined by Altschul et al., (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", *Nucleic Acids Res.*, 25:3389-

3402. The parameters are set to default values, with the exception of the Penalty for mismatch, which is set to -1.

“Stringent” hybridization conditions are sequence dependent and will be different with different environmental parameters (e.g., salt concentrations, and presence of organics). Generally, stringent conditions are selected to be about 5° C. to 20° C. lower than the thermal melting point (T_m) for the specific nucleic acid sequence at a defined ionic strength and pH. Preferably, stringent conditions are about 5° C. to 10° C. lower than the thermal melting point for a specific nucleic acid bound to a perfectly complementary nucleic acid. The T_m is the temperature (under defined ionic strength and pH) at which 50% of a nucleic acid (e.g., tag nucleic acid) hybridizes to a perfectly matched probe.

“Stringent” wash conditions are ordinarily determined empirically for hybridization of each set of tags to a corresponding probe array. The arrays are first hybridized (typically under stringent hybridization conditions) and then washed with buffers containing successively lower concentrations of salts, or higher concentrations of detergents, or at increasing temperatures until the signal to noise ratio for specific to non-specific hybridization is high enough to facilitate detection of specific hybridization. Stringent temperature conditions will usually include temperatures in excess of about 30° C., more usually in excess of about 37° C., and occasionally in excess of about 45° C. Stringent salt conditions will ordinarily be less than about 1000 mM, usually less than about 500 mM, more usually less than about 400 mM, typically less than about 300 mM, preferably less than about 200 mM, and more preferably less than about 150 mM. However, the combination of parameters is more important than the measure of any single parameter. See, e.g., Wetmur et al., *J. Mol. Biol.* 31:349-70 (1966), and Wetmur, *Critical Reviews in Biochemistry and Molecular Biology* 26(34):227-59 (1991).

In a preferred embodiment, “stringent conditions” or “high stringency conditions,” as defined herein, may be hybridization in 50% formamide, 6×SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5×Denhardt’s solution, sonicated salmon sperm DNA (100 µg/ml), 0.5% SDS, and 10% dextran sulfate at 42° C., with washes at 42° C. in 2×SSC (sodium chloride/sodium citrate) and 0.1% SDS at 55° C., followed by a high-stringency wash consisting of 0.2×SSC containing 0.1% SDS at 42° C.

The term “immunoglobulin” (Ig) is used to refer to the immunity-conferring portion of the globulin proteins of serum, and to other glycoproteins, which may not occur in nature but have the same functional characteristics. The term “immunoglobulin” or “Ig” specifically includes “antibodies” (Abs). While antibodies exhibit binding specificity to a specific antigen, immunoglobulins include both antibodies and other antibody-like molecules that lack antigen specificity. Native immunoglobulins are secreted by differentiated B cells termed plasma cells, and immunoglobulins without any known antigen specificity are produced at low levels by the immune system and at increased levels by myelomas. As used herein, the terms “immunoglobulin,” “Ig,” and grammatical variants thereof are used to include antibodies, and Ig molecules without known antigen specificity, or without antigen binding regions.

Native immunoglobulins are usually heterotetrameric glycoproteins of about 150,000 daltons, composed of two identical light (L) chains and two identical heavy (H) chains. Each light chain is linked to a heavy chain by one covalent disulfide bond, while the number of disulfide linkages varies among the heavy chains of different immunoglobulin isotypes. Each

heavy and light chain also has regularly spaced intrachain disulfide bridges. Each heavy chain has at one end a variable domain (V_H) followed by a number of constant domains. Each light chain has a variable domain at one end (V_L) and a constant domain at its other end; the constant domain of the light chain is aligned with the first constant domain of the heavy chain, and the light-chain variable domain is aligned with the variable domain of the heavy chain. Particular amino acid residues are believed to form an interface between the light- and heavy-chain variable domains.

The main Ig isotypes (classes) found in serum, and the corresponding Ig heavy chains, shown in parentheses, are listed below:

IgG (γ chain): the principal Ig in serum, the main antibody raised in response to an antigen, has four major subtypes, several of which cross the placenta;

IgE (ϵ chain): this Ig binds tightly to mast cells and basophils, and when additionally bound to antigen, causes release of histamine and other mediators of immediate hypersensitivity; plays a primary role in allergic reactions, including hay fever, asthma and anaphylaxis; and may serve a protective role against parasites;

IgA (α chain): this Ig is present in external secretions, such as saliva, tears, mucous, and colostrum;

IgM (μ chain): the Ig first induced in response to an antigen; it has lower affinity than antibodies produced later and is pentameric; and

IgD (δ chain): this Ig is found in relatively high concentrations in umbilical cord blood, serves primarily as an early cell receptor for antigen, and is the main lymphocyte cell surface molecule.

Antibodies of the IgG, IgE, IgA, IgM, and IgD isotypes may have the same variable regions, i.e. the same antigen binding cavities, even though they differ in the constant region of their heavy chains. The constant regions of an immunoglobulin, e.g. antibody are not involved directly in binding the antibody to an antigen, but correlate with the different effector functions mediated by antibodies, such as complement activation or binding to one or more of the antibody Fc receptors expressed on basophils, mast cells, lymphocytes, monocytes and granulocytes.

Some of the main antibody isotypes (classes) are divided into further sub-classes. IgG has four known subclasses: IgG₁ (γ_1), IgG₂ (γ_2), IgG₃ (γ_3), and IgG₄ (γ_4), while IgA has two known sub-classes: IgA₁ (α_1) and IgA₂ (α_2).

A light chain of an Ig molecule is either a κ or a λ chain.

The constant region of an immunoglobulin heavy chain is further divided into globular, structurally discrete domains, termed heavy chain constant domains. For example, the constant region of an IgG₁ immunoglobulin heavy chain comprises three constant domains, CH1, CH2 and CH3, and a hinge region between the CH1 and CH2 domains. The IgE immunoglobulin heavy chain comprises four constant domains: CH1, CH2, CH3 and CH4 and does not have a hinge region.

Immunoglobulin sequences, including sequences of immunoglobulin heavy chain constant regions are well known in the art and are disclosed, for example, in Kabat et al., *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institute of Health, Bethesda, Md. (1991). For a discussion of the human IgG₁ heavy chain constant region (γ_1), see also Ellison et al., *Nucl. Acid Res.* 10:4071-4079 (1982); and Takahashi et al., *Cell* 29:671-679 (1982). For a discussion of the human IgG₂ constant region (γ_2), see also Krawinkel et al., *EMBO J.* 1:403-407 (1982); Ellison et al., *Proc. Nat. Acad. Sci. USA* 79:1984-1988 (1982); and Takahashi et al. (1982), supra. For a discussion of

human IgG₃ heavy chain constant region (γ_3), see also Krawinkel et al., (1982), supra, and Takahashi et al. (1982), supra. For a discussion of human IgG₄ heavy chain constant region (γ_4), see also Ellison et al., *DNA* 1:11-18 (1982), Krawinkel et al. (1982), supra, and Takahashi et al. (1982), supra. For a discussion of the human IgE heavy chain constant region (ϵ), see also Max et al., *Cell* 29:691-699 (1982). IgE isoforms are described in Saxon et al., *J. Immunol.* 147:4000 (1991); Peng et al., *J. Immunol.* 148:129-136 (1992); Zhang et al., *J. Exp. Med.* 176:233-243 (1992); and Hellman, *Eur. J. Immunol.* 23:159-167 (1992).

The term "allergen," and grammatical variants thereof, are used to refer to special antigens that are capable of inducing IgE-mediated allergies. An allergen can be almost anything that acts as an antigen and stimulates an IgE-mediated allergic reaction. Common allergens can be found, for example, in food, pollen, mold, house dust which may contain mites as well as dander from house pets, venom from insects such as bees, wasps and mosquitoes.

A "Type I" allergic reaction or "immediate hypersensitivity" or "atopic allergy" occurs when an antigen entering the body encounters mast cells or basophils which have been sensitized by IgE attached to its high-affinity receptor, Fc ϵ RI on these cells. When an allergen reaches the sensitized mast cell or basophil, it cross-links surface-bound IgE, causing an increase in intracellular calcium (Ca²⁺) that triggers the release of pre-formed mediators, such as histamine and proteases, and newly synthesized, lipid-derived mediators such as leukotrienes and prostaglandins. These autocooids produce the clinical symptoms of allergy. In addition, cytokines, e.g. IL-4, TNF-alpha, are released from degranulating basophils and mast cells, and serve to augment the inflammatory response that accompanies an IgE reaction (see, e.g. Immunology, Fifth Edition, Roitt et al., eds., 1998, pp. 302-317).

The terms "vector", "polynucleotide vector", "construct" and "polynucleotide construct" are used interchangeably herein. A polynucleotide vector of this invention may be in any of several forms, including, but not limited to, RNA, DNA, RNA encapsulated in a retroviral coat, DNA encapsulated in an adenovirus coat, DNA packaged in another viral or viral-like form (such as herpes simplex, and adeno-associated virus (AAV)), DNA encapsulated in liposomes, DNA complexed with polylysine, complexed with synthetic polycationic molecules, conjugated with transferrin, complexed with compounds such as polyethylene glycol (PEG) to immunologically "mask" the molecule and/or increase half-life, or conjugated to a non-viral protein. Preferably, the polynucleotide is DNA. As used herein, "DNA" includes not only bases A, T, C, and G, but also includes any of their analogs or modified forms of these bases, such as methylated nucleotides, internucleotide modifications such as uncharged linkages and thioates, use of sugar analogs, and modified and/or alternative backbone structures, such as polyamides.

A "host cell" includes an individual cell or cell culture which can be or has been a recipient of any vector of this invention. Host cells include progeny of a single host cell, and the progeny may not necessarily be completely identical (in morphology or in total DNA complement) to the original parent cell due to natural, accidental, or deliberate mutation and/or change. A host cell includes cells transfected or infected in vivo with a vector comprising a nucleic acid of the present invention.

The term "promoter" means a nucleotide sequence that, when operably linked to a DNA sequence of interest, promotes transcription of that DNA sequence.

Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence.

For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accord with conventional practice.

The term "IgE-mediated biological response" is used to refer to a condition or disease which is characterized by signal transduction through an IgE receptor, including the high-affinity IgE receptor, Fc ϵ RI, and the low-affinity IgE receptor Fc ϵ RII. The definition includes, without limitation, conditions associated with anaphylactic hypersensitivity and atopic allergies, such as, for example, asthma, allergic rhinitis, atopic dermatitis, food allergies, chronic urticaria and angioedema, as well as the serious physiological condition of anaphylactic shock, usually caused by bee stings or medications such as penicillin.

The terms "treat" or "treatment" refer to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) an undesired physiological change or disorder. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, diminishment of extent of disease, stabilized (i.e., not worsening) state of disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether detectable or undetectable. Those in need of treatment include those already with the condition or disorder as well as those prone to have the condition or disorder or those in which the condition or disorder is to be prevented.

"Chronic" administration refers to administration of the agent(s) in a continuous mode as opposed to an acute mode, so as to maintain a desired effect or level of agent(s) for an extended period of time.

"Intermittent" administration is treatment that is not consecutively done without interruption, but rather is periodic in nature.

Administration "in combination with" one or more further therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order.

An "effective amount" is an amount sufficient to effect beneficial or desired therapeutic (including preventative) results. An effective amount can be administered in one or more administrations.

"Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are nontoxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counteri-

ons such as sodium; and/or nonionic surfactants such as TWEEN™, polyethylene glycol (PEG), and PLURONICS™

II. Description of Certain Preferred Embodiments

1. Design of the Fusion Molecules

In one embodiment, the present invention provides fusion molecules that are capable of attenuating a biological response mediated by an FcεR, such as conditions associated with anaphylactic hypersensitivity and atopic allergies, by cross-linking an inhibitory receptor expressed on mast cells and/or basophils with an IgE receptor. The actual sequence of the fusion molecule will depend on the targeted inhibitory receptor, such as an ITIM-containing receptor, e.g. various forms of FcγRIIb, inhibitory members of the gp49 family, especially gp49b1, p91/PIR-B, LAIR-1, LIR-1, or CD22, and on the targeted IgE receptors, e.g. FcεRI or FcεRII.

In a preferred embodiment, the inhibitory receptor is a native low-affinity FcγRIIb receptor, and the IgE receptor is a native high-affinity or low-affinity IgE receptor, i.e. FcεRI or FcεRII, more preferably FcεRI. Accordingly, the first polypeptide sequence present in the fusion molecules binds to the native low-affinity FcγRIIb receptor, while the second polypeptide sequence, which is functionally connected to the first polypeptide sequence, binds to a native FcεRI or FcεRII, preferably FcεRI. When the goal is to cross-link a native FcγRIIb receptor with a native FcεRI receptor by direct binding of the first and second polypeptide sequences present in the single-chain fusion molecules of the invention to the respective receptors, the first and second polypeptide sequences, which are functionally connected, are preferably designed to bind to the respective receptors at essentially the same region(s) as native IgG and IgE, respectively. It has been reported that the CH2-CH3 interface of the IgG Fc domain contains the binding sites for a number of Fc receptors, including the FcγRIIb low-affinity receptor (Wines et al., *J. Immunol.* 164(10):5313-5318 (2000)). Based on FcεRI binding studies, Presta et al., *J. Biol. Chem.* 269:26368-26373 (1994) proposed that six amino acid residues (Arg-408, Ser-411, Lys-415, Glu-452, Arg-465, and Met-469) located in three loops, C-D, E-F, and F-G, computed to form the outer ridge on the most exposed side of the human IgE heavy chain CH3 domain, are involved in binding to the high-affinity receptor FcεRI, mostly by electrostatic interactions. Helm et al., *J. Cell Biol.* 271(13):7494-7500 (1996), reported that the high-affinity receptor binding site in the IgE molecule includes the Pro343-Ser353 peptide sequence within the CH3 domain of the IgE heavy chain, but sequences N- or C-terminal to this core peptide are also necessary to provide structural scaffolding for the maintenance of a receptor binding conformation. In particular, they found that residues, including His, in the C-terminal region of the ε-chain make an important contribution toward the maintenance of the high-affinity of interaction between IgE and FcεRI. The first and second polypeptide sequences within the fusion molecules of the invention are preferably designed to bind to residues within such binding regions.

In another class of the fusion molecules of the invention, the first polypeptide sequence will bind to an ITIM-containing receptor, other than FcγRIIb, expressed on mast cells, basophils and/or B cells. For example, the first polypeptide sequence may contain a region capable of specific binding to an inhibitory member of the gp49 family, such as gp49b1, which is a member of the immunoglobulin superfamily, is preferentially expressed on mast cells and mononuclear macrophages, and contains two ITIM motifs in its cytoplasmic domain. Another ITIM-containing inhibitory receptor is p91,

also referred to as PIR-B, which is known to be expressed on B cells and myeloid lineage cells. Further ITIM-containing receptors that might be targeted by the fusion molecules of the invention include, without limitation, LAIR-1, expressed on B cells, in addition to NK cells, T cells and monocytes; LIR-1, expressed on B cells and monocytes; and CD22 expressed on B cells. For review of ITIM-containing receptors and related art see, e.g. Mustelin et al., *Front. Biosci.* 3:d1060-1096 (1998), and Sinclair et al., 1999, supra.

When the second polypeptide sequence comprises part or whole of a native allergen protein, or a variant thereof, binding between the second polypeptide sequence and an IgE receptor occurs indirectly. The allergen-containing sequence will bind to an allergen-specific IgE molecule bound to a high-affinity IgE receptor (FcεRI) on mast cells or basophils and/or to a low-affinity IgE receptor (FcεRII, CD23) on B lymphocytes. The first, inhibitory receptor-binding, sequence is designed as discussed above. In a preferred embodiment, the allergen part of the molecule is a fragment that contains only a single IgE binding site, in order to avoid antigen cross-linking of IgE on the mast cell surface.

In a preferred embodiment, the first polypeptide sequence present in the fusion molecules of the invention has at least about 80%, more preferably at least about 85%, even more preferably at least about 90%, yet more preferably at least about 95%, most preferably at least about 99% sequence identity with the amino acid sequence of the hinge-CH2-CH3 region of a native IgG, e.g. IgG₁ immunoglobulin, preferably native human IgG₁. In a particularly preferred embodiment, the sequence identity is defined with reference to the human γhinge-CHγ2-CHγ3 sequence of SEQ ID NO: 3.

In another preferred embodiment, the first polypeptide sequence present in the fusion molecules of the invention has at least about 80%, more preferably at least about 85%, even more preferably at least about 90%, yet more preferably at least about 95%, most preferably at least about 99% sequence identity with the amino acid sequence of a native ligand of another ITIM-containing receptor expressed on mast cells, basophils and/or B cells, such as gp49b1 or p91/PIR-B (a cytoplasmic signaling protein activated by IFN-α, IFN-γ, and IL-6), or mast cell function Ag.

In yet another preferred embodiment, the first polypeptide sequence present in the fusion molecules of the invention has at least about 80%, more preferably at least about 85%, even more preferably at least about 90%, yet more preferably at least about 95%, most preferably at least about 99% sequence identity with the amino acid sequence of c-Kit (see, e.g. Yarden et al., *EMBO J.* 6:3341-51 (1987)).

The second polypeptide sequence present in the fusion molecules of the invention preferably has at least about 80%, more preferably at least about 85%, even more preferably at least about 90%, yet more preferably at least about 95%, most preferably at least about 99% sequence identity with the amino acid sequence of the CH2-CH3-CH4 region of a native IgE immunoglobulin, preferably native human IgE, or with the sequence of a native allergen protein. In a particularly preferred embodiment, the sequence identity is defined with reference to the human CHε2-CHε3-CHε4 sequence of SEQ ID NO: 6 or with regard to one of the allergen sequences listed in Table 1 below (SEQ ID NOS: 7 through 173), or, in a preferred embodiment, one of two Ara h2 clones represented by SEQ ID NOS: 174 and 175, respectively.

Alternatively, the first polypeptide sequence present in the fusion molecules of the invention may comprise a sequence encoded by nucleic acid hybridizing under stringent conditions to the complement of the coding sequence of a native γhinge-CHγ2-CHγ3 sequence, preferably the γhinge-CHγ2-

CH₃ coding sequence from within SEQ ID NO: 1, or with the coding sequence of another immunoglobulin heavy chain constant region sequence required for IgG binding.

When the first polypeptide sequence binds specifically to an ITIM-containing receptor expressed on mast cells, basophils or B cells, it is preferably encoded by nucleic acid hybridizing under stringent conditions to the complement of the coding sequence of a native ligand of that receptor.

Similarly, the second polypeptide sequence present in the fusion molecules of the invention may comprise a sequence encoded by nucleic acid hybridizing under stringent conditions to the complement of the coding sequence of a native CH₂-CH₃-CH₄ sequence, preferably the CH₂-CH₃-CH₄ coding sequence from within SEQ ID NO: 4, or to the complement of the coding sequence of a native allergen, such as those listed in Table 1.

Whenever the first and/or second polypeptide sequence included in the fusion molecules of the invention is an amino acid variant of a native immunoglobulin constant region sequence, it is required to retain the ability to bind to the corresponding native receptor, such as a native IgG inhibitory receptor (e.g. FcγRIIb) and a native high-affinity IgE receptor (e.g. FcεRI) or native low-affinity IgE receptor (FcεRII, CD23), respectively. As discussed above, the receptor binding domains within the native IgG and IgE heavy chain constant region sequences have been identified. Based on this knowledge, the amino acid sequence variants may be designed to retain the native amino acid residues essential for receptor binding, or to perform only conservative amino acid alterations (e.g. substitutions) at such residues.

In making amino acid sequence variants that retain the required binding properties of the corresponding native sequences, the hydrophatic index of amino acids may be considered. For example, it is known that certain amino acids may be substituted for other amino acids having a similar hydrophatic index or score without significant change in biological activity. Thus, isoleucine, which has a hydrophatic index of +4.5, can generally be substituted for valine (+4.2) or leucine (+3.8), without significant impact on the biological activity of the polypeptide in which the substitution is made. Similarly, usually lysine (-3.9) can be substituted for arginine (-4.5), without the expectation of any significant change in the biological properties of the underlying polypeptide.

Other considerations for choosing amino acid substitutions include the similarity of the side-chain substituents, for example, size, electrophilic character, charge in various amino acids. In general, alanine, glycine and serine; arginine and lysine; glutamate and aspartate; serine and threonine; and valine, leucine and isoleucine are interchangeable, without the expectation of any significant change in biological properties. Such substitutions are generally referred to as conservative amino acid substitutions, and, as noted above, are the preferred type of substitutions within the polypeptides of the present invention.

Alternatively or in addition, the amino acid alterations may serve to enhance the receptor binding properties of the fusion molecules of the invention. Variants with improved receptor binding and, as a result, superior biological properties can be readily designed using standard mutagenesis techniques, such as alanine-scanning mutagenesis, PCR mutagenesis or other mutagenesis techniques, coupled with receptor binding assays, such as the assay discussed below or described in the Example.

In a preferred embodiment, the fusion molecules of the present invention comprise a first polypeptide sequence including functionally active hinge, CH₂ and CH₃ domains of the constant region of an IgG₁ heavy chain (γhinge-CH₂-

CH₃ sequence) linked at its C-terminus to the N-terminus of a second polypeptide including functionally active CH₂, CH₃ and CH₄ domains of the constant region of an IgE heavy chain (CH₂-CH₃-CH₄ sequence). In a particularly preferred embodiment, the first polypeptide sequence is composed of functionally active hinge, CH₂ and CH₃ regions of a native human IgG₁ heavy chain, linked at its C-terminus to the N-terminus of a second polypeptide composed of functionally active CH₂, CH₃ and CH₄ domains of a native human IgE heavy chain constant region.

While it is preferred to fuse the IgG heavy chain constant region sequence (or a homologous sequence) C-terminally to the N-terminus of the IgE heavy chain constant region sequence (or a homologous sequence), fusion molecules in which the IgE heavy chain constant region sequence (or a homologous sequence) is fused C-terminally to the N-terminus of the IgG heavy chain constant region sequence (or a homologous sequence) are also within the scope of the invention. The fusion molecules may also comprise repeats of identical or different IgG and/or IgE heavy chain constant region sequences. For example, two repeats of IgG heavy chain constant region sequences; each including an IgG inhibitory receptor-binding domain, can be followed by IgE heavy chain constant region sequences (GGE structure), or two repeats of identical or different IgG heavy chain constant region sequences may flank an IgE heavy chain constant region sequence (GEG structure), etc. Fusion molecules comprising more than one binding sequence for a target receptor (e.g. an FcγRIIb receptor) are expected to have superior biological, e.g. anti-allergic properties.

The same considerations apply to the structure of fusion molecules where the second polypeptide sequence comprises, is or is derived from an allergen protein. Such molecules may also include repeats of the IgG heavy chain constant region sequences, fused to either or both sides of the allergen sequence.

Similarly, molecules in which the first polypeptide sequence binds to a different inhibitory receptor expressed on mast cells and/or basophils, e.g. an ITIM-containing inhibitory receptor functionally connected to a second polypeptide sequence binding directly or indirectly to an IgE receptor, e.g. FcεRI, may contain multiple repeats of the inhibitory receptor binding regions and/or the IgE binding regions.

In all embodiments, the two polypeptide sequences are functionally connected, which means that they retain the ability to bind to the respective native receptors, such as a native IgG inhibitory receptor, e.g. a low-affinity FcγRIIb receptor, and to a native high-affinity IgE receptor, e.g. FcεRI or low-affinity IgE receptor, as desired. As a result, the fusion molecules, comprising the first and second polypeptide sequences functionally connected to each other, are capable of cross-linking the respective native receptors, such as FcγRIIb and FcεRI or FcγRIIb and FcεRII. In order to achieve a functional connection between the two binding sequences within the fusion molecules of the invention, it is preferred that they retain the ability to bind to the corresponding receptor with a binding affinity similar to that of a native immunoglobulin ligand of that receptor.

The fusion molecules of the present invention are typically produced and act as homodimers or heterodimers, comprising two of the fusion molecules hereinabove described covalently linked to each other. The covalent attachment is preferably achieved via one or more disulfide bonds. For example, the prototype protein designated GE2 is produced as a homodimer composed of the two γhinge-CH₂-CH₃-15aa linker-CH₂-CH₃-CH₄ chains connected to each other by interchain disulfide bonds, to provide an immuno-

globulin-like structure. It is also possible to produce heterodimers, in which two different fusion molecules are linked to each other by one or more covalent linkages, e.g. disulfide bond(s). Such bifunctional structures might be advantageous in that they are able to cross-link the same or different IgE(s) with different inhibitory receptors.

Receptor binding can be tested using any known assay method, such as competitive binding assays, direct and indirect sandwich assays. Thus, binding of a first polypeptide sequence included in the fusion molecules herein to a low-affinity IgG inhibitory receptor, or the binding of a second polypeptide sequence included herein to a high-affinity or low-affinity IgE receptor can be tested using conventional binding assays, such as competitive binding assays, including RIAs and ELISAs. Ligand/receptor complexes can be identified using traditional separation methods as filtration, centrifugation, flow cytometry, and the results from the binding assays can be analyzed using any conventional graphical representation of the binding data, such as Scatchard analysis. The assays may be performed, for example, using a purified receptor, or intact cells expressing the receptor. One or both of the binding partners may be immobilized and/or labeled. A particular cell-based binding assay is described in the Example below.

The two polypeptide sequences present in the fusion molecules of the invention may be associated with one another by any means that allows them to cross-link the relevant receptors. Thus, association may take place by a direct or indirect covalent linkage, where "indirect" covalent linkage means that the two polypeptide sequences are part of separate molecules that interact with one another, either directly or indirectly. For example, each polypeptide sequence can be directly linked to one member of an interacting pair of molecules, such as, for example, a biotin/avidin pair. Alternatively, the two polypeptide sequences can be linked using a "dimerizer" system based on linkage to an entity that associates with a common ligand, such as dimerizer systems based on cyclosporin, FK506, rapamycin, countermycin, and the like.

In a preferred embodiment, the first and second polypeptide sequences, such as, for example, two immunoglobulin constant region segments, or an immunoglobulin constant region sequence and an allergen sequence, are connected by a polypeptide linker. The polypeptide linker functions as a "spacer" whose function is to separate the functional receptor binding domains, or the Fc ϵ R receptor binding domain and the IgE-binding sequence in the allergen, so that they can independently assume their proper tertiary conformation. The polypeptide linker usually comprises between about 5 and about 25 residues, and preferably contains at least about 10, more preferably at least about 15 amino acids, and is composed of amino acid residues which together provide a hydrophilic, relatively unstructured region. Linking amino acid sequences with little or no secondary structure work well. The specific amino acids in the spacer can vary, however, cysteines should be avoided. Suitable polypeptide linkers are, for example, disclosed in WO 88/09344 (published on Dec. 1, 1988), as are methods for the production of multifunctional proteins comprising such linkers.

In a less preferred embodiment, the IgG and IgE constant region sequences, the IgG constant region sequences and the allergen sequences, or sequences showing high degree of sequence identity with such sequences, may be directly fused to each other, or connected by non-polypeptide linkers. Such linkers may, for example, be residues of covalent bifunctional cross-linking agents capable of linking the two sequences without the impairment of the receptor (antibody) binding

function. The bifunctional cross-linking reagents can be divided according to the specificity of their functional groups, e.g. amino, sulphydryl, guanidino, indole, carboxyl specific groups. Of these, reagents directed to free amino groups have become especially popular because of their commercial availability, ease of synthesis and the mild reaction conditions under which they can be applied. A majority of heterobifunctional cross-linking reagents contains a primary amine-reactive group and a thiol-reactive group (for review, see Ji, T. H. "Bifunctional Reagents" in: *Meth. Enzymol.* 91:580-609 (1983)).

In a further specific embodiment, the two polypeptide sequences (including variants of the native sequences) are dimerized by amphiphilic helices. It is known that recurring copies of the amino acid leucine (Leu) in gene regulatory proteins can serve as teeth that "zip" two protein molecules together to provide a dimer. For further details about leucine zippers, which can serve as linkers for the purpose of the present invention, see for example: Landschulz, W. H., et al. *Science* 240:1759-1764 (1988); O'Shea, E. K. et al., *Science* 243: 38-542 (1989); McKnight, S. L., *Scientific American* 54-64, April 1991; Schmidt-Dorr, T. et al., *Biochemistry* 30:9657-9664 (1991); Blondel, A. and Bedouelle, H. *Protein Engineering* 4:457-461 (1991), and the references cited in these papers.

In a different approach, the two polypeptide sequences (including variants of the native sequences) are linked via carbohydrate-directed bifunctional cross-linking agents, such as those disclosed in U.S. Pat. No. 5,329,028.

The cross-linking of an inhibitory receptor expressed on mast cells and/or basophils, such as an ITIM-containing receptor, including IgG inhibitory receptors, e.g. Fc γ RIIb and a high-affinity IgE receptor, e.g. Fc ϵ RI or low-affinity IgE receptor, e.g. Fc ϵ RII, inhibit Fc ϵ R mediated biological responses. Such biological responses preferably are the mediation of an allergic reactions or autoimmune reactions via Fc ϵ R, including, without limitation, conditions associated with IgE mediated reactions, such as, for example, asthma, allergic rhinitis, food allergies, chronic urticaria and angioedema, allergic reactions to hymenophthera (e.g. bee and yellow jacket) stings or medications such as penicillinup to and including the severe physiological reaction of anaphylactic shock.

2. Preparation of the Fusion Molecules

When the fusion molecules are polypeptides, in which the first and second polypeptide sequences are directly fused or functionally connected by a polypeptide linker, they can be prepared by well known methods of recombinant DNA technology or traditional chemical synthesis. If the polypeptides are produced by recombinant host cells, cDNA encoding the desired polypeptide of the present invention is inserted into a replicable vector for cloning and expression. As discussed before, the nucleotide and amino acid sequences of native immunoglobulin constant regions, including native IgG and IgE constant region sequences, are well known in the art and are readily available, for example, from Kabat et al., *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institute of Health, Bethesda, Md. (1991).

Similarly, the sequences of a large number of allergens are well known in the art. According to a nomenclature system established for allergens by the WHO/IUIS Allergen Nomenclature Subcommittee, the designation of any particular allergen is composed of the first three letters of the genus; a space; the first letter of the species name; a space and an arabic number. In the event that two species names have identical designations, they are discriminated from one another by

adding one or more letters to each species designation. Using this designation, the allergen Aln G 1 is a major pollen allergen from the genus *Alnus* and the species *glutinosa*, the sequence of which is available from the SWISS-PROT database under the entry name MPAG_ALNGL (Primary Accession number: P38948) (Breitender et al., *J. Allergy Clin. Immunol.* 90:909-917 (1992)). A list of known antigens, including their origin, entry name and Primary Accession Number in the SWISS-PROT database is provided in Table 1. The molecular weight of most food allergens is between 10,000 and 70,000 Da. Some allergens, such as Ara h 1 (63.5 kDa) and Ara h 2 (17 kDa), occur as polymers that are larger, e.g. 200 to 300 kDa.

As noted earlier, it might be advantageous to use in the fusion molecules of the present invention a fragment of a native or variant allergen that contains only a single IgE-binding site. For many of the allergen proteins listed in Table 1, the IgE-binding sites have been determined. For example, the IgE-binding epitopes of Par j 2, a major allergen of *Parietaria judaica* pollen, have been determined by Costa et al., *Allergy* 55:246-50 (2000). The IgE-binding epitopes of major peanut antigens Ara h 1 (Burks et al., *Eur. J. Biochem.* 254:334-9 (1997)); Ara h 2 (Stanley et al., *Arch Biochem. Biophys.* 342:244-53 (1997)); and Ara h 3 (Rabjohn et al., *J. Clin. Invest.* 103:535-42 (1999)) are also known, just to mention a few.

TABLE 1

Allergen	SWISS-PROT Entry	SWISS-PROT Accession No.	Protein Name	Source	SEQ ID NO.
Aln g 1	MPAG_ALNGL	P38948	Major Pollen Allergen Aln g 1	Pollen of <i>Alnus glutinosa</i> (Alder)	8
Alt a 6	RLA2_ALTAL	P42037	60S Acidic Ribosomal Protein P2	<i>Alternaria alternata</i>	9
Alt a 7	ALA7_ALTAL	P42058	Minor Allergen Alt a 7	<i>Alternaria alternata</i>	10
Alt a 10	DHAL_ALTAL	P42041	Aldehyde Dehydrogenase	<i>Alternaria alternata</i>	11
Alt a 12	RLA1_ALTAL	P49148	60S Acidic Ribosomal Protein P1	<i>Alternaria alternata</i>	12
Amb a 1	MP11_AMBAR	P27759	Pollen Allergen Amb a 1.1 [Precursor]	<i>Ambrosia artemisiifolia</i> (Short ragweed)	13
Amb a 1	MP12_AMBAR	P27760	Pollen Allergen Amb a 1.2 [Precursor]	<i>Ambrosia artemisiifolia</i> (Short ragweed)	14
Amb a 1	MP13_AMBAR	P27761	Pollen Allergen Amb a 1.3 [Precursor]	<i>Ambrosia artemisiifolia</i> (Short ragweed)	15
Amb a 1	MP14_AMBAR	P28744	Pollen Allergen Amb a 1.4 [Precursor]	<i>Ambrosia artemisiifolia</i> (Short ragweed)	16
Amb a 2	MPA2_AMBAR	P27762	Pollen Allergen Amb a 2 [Precursor]	<i>Ambrosia artemisiifolia</i> (Short ragweed)	17
Amb a 3	MPA3_AMBEL	P00304	Pollen Allergen Amb a 3	<i>Ambrosia artemisiifolia</i> var. <i>elatior</i> (Short ragweed)	18
Amb a 5	MPA5_AMBEL	P02878	Pollen Allergen Amb a 5	<i>Ambrosia artemisiifolia</i> var. <i>elatior</i> (Short ragweed)	19
Amb p 5	MPA5_AMBPS	P43174	Pollen Allergen Amb p 5-a [Precursor]	<i>Ambrosia psilostachya</i> (Western ragweed)	20
Amb p 5	MP5B_AMBPS	P43175	Pollen Allergen Amb p 5b [Precursor]	<i>Ambrosia psilostachya</i> (Western ragweed)	21
Amb t 5	MPT5_AMBTR	P10414	Pollen Allergen Amb t 5 [Precursor]	<i>Ambrosia trifida</i> (Giant ragweed)	22
Api g 1	MPAG_APIGR	P49372	Major Allergen Api g	<i>Apium graveolens</i> (Celery)	23
Api m 1	PA2_APIME	P00630	Phospholipase A2 [Precursor] [Fragment]	<i>Apis mellifera</i> (Honeybee)	24
Api m 2	HUGA_APIME	Q08169	Hyaluronoglucosaminidase [Precursor]	<i>Apis mellifera</i> (Honeybee)	25
Api m 3	MEL_APIME	P01501	Melittin [Precursor]	<i>Apis mellifera</i> (Honeybee) <i>Apis cerana</i> (Indian honeybee)	26
Ara h 1	AH11_ARAHY	P43237	Allergen Ara h 1, Clone P17	<i>Arachis hypogaea</i> (Peanut)	27
Ara h 1	AH12_ARAHY	P43238	Allergen Ara h 1, Clone P41b	<i>Arachis hypogaea</i> (Peanut)	28
Ara t 8	PRO1_ARATH	Q42449	Profilin 1	<i>Arabidopsis thaliana</i> (Mouse-ear cress)	29

TABLE 1-continued

Allergen	SWISS-PROT Entry	SWISS-PROT Accession No.	Protein Name	Source	SEQ ID NO.
Asp f 1	RNMG_ASPRE	P04389	Ribonuclease Mitogillin [Precursor]	<i>Aspergillus restrictus</i> ; <i>Aspergillus fumigatus</i> (<i>Sartorya fumigata</i>)	30
Asp f 2	MAF2_ASPFU	P79017	Major Allergen Asp f 2 [Precursor]	<i>Aspergillus fumigatus</i> (<i>Sartorya fumigata</i>)	31
Asp f 3	PM2O_ASPFU	O43099	Probable Peroxisomal Membrane Protein PMP20	<i>Aspergillus fumigatus</i> (<i>Sartorya fumigata</i>)	32
Asp f 13	AF13_ASPFU	O60022	Allergen Asp f 13 [Precursor]	<i>Aspergillus fumigatus</i> (<i>Sartorya fumigata</i>)	33
Bet v 1	BV1A_BETVE	P15494	Major Pollen Allergen Bet v 1-a	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	34
Bet v 1	BV1C_BETVE	P43176	Major Pollen Allergen Bet v 1-c	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	35
Bet v 1	BV1D_BETVE	P43177	Major Pollen Allergen Bet v 1-d/h	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	36
Bet v 1	BV1E_BETVE	P43178	Major Pollen Allergen Bet v 1-e	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	37
Bet v 1	BV1F_BETVE	P43179	Major Pollen Allergen Bet v 1-f/i	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	38
Bet v 1	BV1G_BETVE	P43180	Major Pollen Allergen Bet v 1-g	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	39
Bet v 1	BV1J_BETVE	P43183	Major Pollen Allergen Bet v 1-j	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	40
Bet v 1	BV1K_ETVE	P43184	Major Pollen Allergen Bet v 1-k	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	41
Bet v 1	BV1L_BETVE	P43185	Major Pollen Allergen Bet v 1-1	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	42
Bet v 1	BV1M_BETVE	P43186	Major Pollen Allergen Bet v 1-m/n	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	43
Bet v 2	PROF-BETVE	P25816	Profilin	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	44
Bet v 3	BTV3_BETVE	P43187	Allergen Bet v 3	<i>Betula verrucosa</i> (White birch) (<i>Betula pendula</i>)	45
Bla g 2	ASP2_BLAGE	P54958	Aspartic Protease Bla g 2 [Precursor]	<i>Blattella germanica</i> (German cockroach)	46
Bla g 4	BLG4_BLAGE	P54962	Allergen Bla g 4 [Precursor]	<i>Blattella germanica</i> (German cockroach)	47
Bla g 5	GTS1_BLAGE	O18598	Glutathione-S-transferase	<i>Blattella germanica</i> (German cockroach)	48
Blo t 12	BT12_BLOTA	Q17282	Allergen Blo t 12 [Precursor]	<i>Blomia tropicalis</i> (Mite)	49
Bos d 2	ALL2_BOVIN	Q28133	Allergen Bos d 2 [Precursor]	<i>Bos taurus</i> (Bovine)	50
Bos d 5	LACB_BOVIN	P02754	Beta-lactoglobulin [Precursor]	<i>Bos taurus</i> (Bovine)	51
Bra j 1	ALL1_BRAJU	P80207	Allergen Bra j 1-e, Small and Large Chains	<i>Brassica juncea</i> (Leaf mustard) (Indian mustard)	52
Can a 1	ADH1_CANAL	P43067	Alcohol Dehydrogenase 1	<i>Candida albicans</i> (Yeast)	53
Can f 1	ALL1_CANFA	O18873	Major Allergen Can f 1 [Precursor]	<i>Canis familiaris</i> (Dog)	54
Can f 2	ALL2_CANFA	O18874	Minor Allergen Can f 2 [Precursor]	<i>Canis familiaris</i> (Dog)	55
Car b 1	MPA1_CARBE	P38949	Major Pollen Allergen Car b 1, Isoforms 1A and 1B	<i>Carpinus betulus</i> (Hornbeam)	56

TABLE 1-continued

Allergen	SWISS-PROT Entry	SWISS-PROT Accession No.	Protein Name	Source	SEQ ID NO.
Car b 1	MPA2_CARBE	P38950	Major Pollen Allergen Car b 1, Isoform 2	<i>Carpinus betulus</i> (Hornbeam)	57
Cha o 1	MPA1_CHAOB	Q96385	Major Pollen Allergen Cha o 1 [Precursor]	<i>Chamaecyparis obtusa</i> (Japanese cypress)	58
Cla h 3	DHAL_CLAHE	P40108	Aldehyde Dehydrogenase	<i>Cladosporium herbarum</i>	59
Cla h 3	RLA3_CLAHE	P42038	60S Acidic Ribosomal Protein P2	<i>Cladosporium herbarum</i>	60
Cla h 4	HS70_CLAHE	P40918	Heat Shock 70 KDa Protein	<i>Cladosporium herbarum</i>	61
Cla h 4	RLA4_CLAHE	P42039	60S Acidic Ribosomal Protein P2	<i>Cladosporium herbarum</i>	62
Cla h 5	CLH5_CLAHE	P42059	Minor Allergen Cla h 5	<i>Cladosporium herbarum</i>	63
Cla h 6	ENO_CLAHE	P42040	Enolase	<i>Cladosporium herbarum</i>	64
Cla h 12	RLA1_CLAHE	P50344	60S Acidic Ribosomal Protein P1	<i>Cladosporium herbarum</i>	65
Cop c 2 Cor a 1	THIO_CAPCM MPAA_CORAV	Q08407	Major Pollen Allergen Cor a 1, Isoforms 5, 6, 11 and 16	<i>Corylus avellana</i> (European hazel)	66
Cup a 1	MPA1_CUPAR	Q9SCG9	Major Pollen Allergen Cup a 1	<i>Cupressus arizonica</i>	67
Cry j 1	SBP_CRYJA	P18632	Sugi Basic Protein [Precursor]	<i>Cryptometia japonica</i> (Japanese cedar)	68
Cry j 2	MPA2_CRYJA	P43212	Possible Polygalacturonase	<i>Cryptomeria japonica</i> (Japanese cedar)	69
Cyn d 12	PROF_CYNDA	004725	Profilin	<i>Cynodon dactylon</i> (Bermuda grass)	70
Dac g 2	MPG2_DACGL	Q41183	Pollen Allergen Dac g 2 [Fragment]	<i>Dactylis glomerata</i> (Orchard grass) (Cocksfoot grass)	71
Dau c 1	DAUI_DAUCA	O04298	Major Allergen Dau c 1	<i>Daucus carota</i> (Carrot)	72
Der f 1	MMAL_DERFA	P16311	Major Mite Fecal Allergen Der f 1 [Precursor]	<i>Dermatophagoides farinae</i> (House-dust mite)	73
Der f 2	DEF2_DERFA	Q00855	Mite Allergen Der f 2 [Precursor]	<i>Dermatophagoides farinae</i> (House-dust mite)	74
Der f 3	DEF3_DERFA	P49275	Mite Allergen Der f 3 [Precursor]	<i>Dermatophagoides farinae</i> (House-dust mite)	75
Der f 6	DEF6_DERFA	P49276	Mite Allergen Der f 6 [Fragment]	<i>Dermatophagoides farinae</i> (House-dust mite)	76
Der f 7	DEF7_DERFA	Q26456	Mite Allergen Der f 7 [Precursor]	<i>Dermatophagoides farinae</i> (House-dust mite)	77
Der m 1	MMAL_DERMI	P16312	Major Mite Fecal Allergen Der m 1 [Fragment]	<i>Dermatophagoides microceras</i> (House-dust mite)	78
Der p 1	MMAL_DERPT	P08176	Major Mite Fecal Allergen Der p 1 [Precursor]	<i>Dermatophagoides pteronyssinus</i> (House-dust mite)	79
Der p 2	DER2_DERPT	P49278	Mite Allergen Der p 2 [Precursor]	<i>Dermatophagoides pteronyssinus</i> (House-dust mite)	80
Der p 3	DER3_DERPT	P39675	Mite Allergen Der p 3 [Precursor]	<i>Dermatophagoides pteronyssinus</i> (House-dust mite)	81
Der p 4	AMY_DERPT	P49274	Alpha-Amylase [Fragment]	<i>Dermatophagoides pteronyssinus</i> (House-dust mite)	82
Der p 5	DER5_DERPT	P14004	Mite Allergen Der p 5	<i>Dermatophagoides pteronyssinus</i> (House-dust mite)	83
Der p 6	DER6_DERPT	P49277	Mite Allergen Der p 6 [Fragment]	<i>Dermatophagoides pteronyssinus</i> (House-dust mite)	84

TABLE 1-continued

Allergen	SWISS-PROT Entry	SWISS-PROT Accession No.	Protein Name	Source	SEQ ID NO.
Der p 7	DER7_DERPT	P49273	Mite Allergen Der p7 [Precursor]	<i>Dermatophagoides pteronyssinus</i> (House-dust mite)	85
Dol a 5	VA5_DOLAR	Q05108	Venom Allergen 5	<i>Dolichovespula arenaria</i> (Yellow hornet)	86
Dol m 1	PA11_DOLMA	Q06478	Phospholipase A1 1 [Precursor] [Fragment]	<i>Dolichovespula maculata</i> (White-face hornet) (Bald-faced hornet)	87
Dol m 1	PA12_DOLMA	P53357	Phospholipase A1 2	<i>Dolichovespula maculata</i> (White-face hornet) (Bald-faced hornet)	88
Dol m 2	HUGA_DOLMA	P49371	Hyaluronoglucosaminidase	<i>Dolichovespula maculata</i> (White-face hornet) (Bald-faced hornet)	89
Dol m 5	VA52_DOLMA	P10736	Venom Allergen 5.01 [Precursor]	<i>Dolichovespula maculata</i> (White-face hornet) (Bald-faced hornet)	90
Dol m 5	VA53_DOLMA	P10737	Venom Allergen 5.02 [Precursor] [Fragment]	<i>Dolichovespula maculata</i> (White-face hornet) (Bald-faced hornet)	91
Equ c 1	ALL1_HORSE	Q95182	Major Allergen Equ c 1 [Precursor]	<i>Equus caballus</i> (Horse)	92
Equ c 2	AL21_HORSE	P81216	Dander major Allergen Equ c 2.0101 [Fragment]	<i>Equus caballus</i> (Horse)	93
Equ c 2	AL22_HORSE	P81217	Dander Major Allergen Equ c 2.0102 [Fragment]	<i>Equus caballus</i> (Horse)	94
Eur m 1	EUM1_EURMA	P25780	Mite Group I Allergen Eur m 1 [Fragment]	<i>Euroglyphus maynei</i> (House-dust mite)	95
Fel d 1	FELA_FELCA	P30438	Major Allergen I Polypeptide Chain 1 Major Form [Precursor]	<i>Felis silvestris catus</i> (Cat)	96
Fel d 1	FELB_FELCA	P30439	Major Allergen I Polypeptide Chain 1 Minor Form [Precursor]	<i>Felis silvestris catus</i> (Cat)	97
Fel d 1	FEL2_FELCA	P30440	Major Allergen I Polypeptide Chain 2 [Precursor]	<i>Felis silvestris catus</i> (Cat)	98
Gad c 1	PRVB_GADCA	P02622	Parvalbumin Beta	<i>Gadus callarias</i> (Baltic cod)	99
Gal d 1	IOVO_CHICK	P01005	Ovomucoid [Precursor]	<i>Gallus gallus</i> (Chicken)	100
Gal d 2	OVAL_CHICK	P01012	Ovalbumin	<i>Gallus gallus</i> (Chicken)	101
Gal d 3	TRFE_CHICK	P02789	Ovotransferrin [Precursor]	<i>Gallus gallus</i> (Chicken)	102
Gal d 4	LYC_CHICK	P00698	Lysozyme C [Precursor]	<i>Gallus gallus</i> (Chicken)	103
Hel a 2	PROF_HELAN	O81982	Profilin	<i>Helianthus annuus</i> (Common sunflower)	104
Hev b 1	REF_HEVBR	P15252	Rubber Elongation Factor Protein	<i>Hevea brasiliensis</i> (Para rubber tree)	105
Hev b 5	HEV5_HEVBR	Q39967	Major Latex Allergen Hev b 5	<i>Hevea brasiliensis</i> (Para rubber tree)	106
Hol 1 1	MPH1_HOLLA	P43216	Major Pollen Allergen Hol 1 1 [Precursor]	<i>Holcus lanatus</i> (Velvet grass)	107
Hor v 1	IAA1_HORVU	P16968	Alpha-amylase Inhibitor Bmai-1 [Precursor] [Fragment]	<i>Hordeum vulgare</i> (Barley)	108
Jun a 1	MPA1_JUNAS	P81294	Major Pollen Allergen Jun a 1 [Precursor]	<i>Juniperus ashei</i> (Ozark white cedar)	109

TABLE 1-continued

Allergen	SWISS-PROT Entry	SWISS-PROT Accession No.	Protein Name	Source	SEQ ID NO.
Jun a 3	PRR3_JUNAS	P81295	Pathogenesis-Related Protein [Precursor]	<i>Juniperus ashei</i> (Ozark white cedar)	110
Lep d 1	LEPI_LEPDS	P80384	Mite Allergen Lep d 1 [Precursor]	<i>Lepidoglyphus destructor</i> (Storage mite)	111
Lol p 1	MPLI_LOLPR	P14946	Pollen Allergen Lol p 1 [Precursor]	<i>Lolium perenne</i> (Perennial ryegrass)	112
Lol p 2	MPL2_LOLPR	P14947	Pollen Allergen Lol p 2-a	<i>Lolium perenne</i> (Perennial ryegrass)	113
Lol p 3	MPL3_LOLPR	P14948	Pollen Allergen Lol p 3	<i>Lolium perenne</i> (Perennial ryegrass)	114
Lol p 5	MP5A_LOLPR	Q40240	Major Pollen Allergen Lol p 5a [Precursor]	<i>Lolium perenne</i> (Perennial ryegrass)	115
Lol p 5	MP5B_LOLPR	Q40237	Major Pollen Allergen Lol p 5b [Precursor]	<i>Lolium perenne</i> (Perennial ryegrass)	116
Mal d 1	MALI_MALDO	P43211	Major Allergen Mal d 1	<i>Malus domestica</i> (Apple) (<i>Malus sylvestris</i>)	117
Mer a 1	PROF_MERAN	O49894	Profilin	<i>Mercurialis annua</i> (Annual mercury)	118
Met e 1	TPM1_METEN	Q25456	Tropomyosin	<i>Metapenaeus ensis</i> (Greasyback shrimp) (Sand shrimp)	119
Mus m 1	MUP6_MOUSE	P02762	Major Urinary Protein 6 [Precursor]	<i>Mus musculus</i> (Mouse)	120
Myr p 1	MYR1_MYRPI	Q07932	Major Allergen Myr p 1 [Precursor]	<i>Myrmecia pilosula</i> (Bulldog ant) (Australian jumper ant)	121
Myr p 2	MYR2_MYRPI	Q26464	Allergen Myr p 2 [Precursor]	<i>Myrmecia pilosula</i> (Bulldog ant) (Australian jumper ant)	122
Ole e 1	ALL1_OLEEU	P19963	Major Pollen Allergen	<i>Olea europaea</i> (Common olive)	123
Ole e 4	ALL4_OLEEU	P80741	Major Pollen Allergen Ole e 4 [Fragments]	<i>Olea europaea</i> (Common olive)	124
Ole e 5	SODC_OLEEU	P80740	Superoxide Dismutase [CU-ZN] [Fragment]	<i>Olea europaea</i> (Common olive)	125
Ole e 7	ALL7_OLEEU	P81430	Pollen Allergen Ole e 7 [Fragment]	<i>Olea europaea</i> (Common olive)	126
Ory s 1	MPO1_ORYSA	Q40638	Major Pollen Allergen Ory s 1 [Precursor]	<i>Oryza sativa</i> (Rice)	127
Par j 1	NL11_PARJU	P43217	Probable Nonspecific Lipid-Transfer Protein [Fragment]	<i>Parietaria judaica</i>	128
Par j 1	NL12_PARJU	O04404	Probable Nonspecific Lipid-Transfer Protein 1 [Precursor]	<i>Parietaria judaica</i>	129
Par j 1	NL13_PARJU	Q40905	Probable Nonspecific Lipid-Transfer Protein 1 [Precursor]	<i>Parietaria judaica</i>	130
Par j 2	NL21_PARJU	P55958	Probable Nonspecific Lipid-Transfer Protein 2 [Precursor]	<i>Parietaria judaica</i>	131
Par j 2	NL22_PARJU	O04403	Probable Nonspecific Lipid-Transfer Protein 2 [Precursor]	<i>Parietaria judaica</i>	132
Pha a 1	MPA1_PHAAQ	Q41260	Major Pollen Allergen Pha a 1 [Precursor]	<i>Phalaris aquatica</i> (Canary grass)	133
Pha a 5	MP51_PHAAQ	P56164	Major Pollen Allergen Pha a 5.1 [Precursor]	<i>Phalaris aquatica</i> (Canary grass)	134
Pha a 5	MP52_PHAAQ	P56165	Major Pollen Allergen Pha a 5.2 [Precursor]	<i>Phalaris aquatica</i> (Canary grass)	135
Pha a 5	MP53_PHAAQ	P56166	Major Pollen Allergen Pha a 5.3 [Precursor]	<i>Phalaris aquatica</i> (Canary grass)	136
Pha a 5	MP54_PHAAQ	P56167	Major Pollen Allergen Pha a 5.4 [Fragment]	<i>Phalaris aquatica</i> (Canary grass)	137

TABLE 1-continued

Allergen	SWISS-PROT Entry	SWISS-PROT Accession No.	Protein Name	Source	SEQ ID NO.
Phl p 1	MPP1_PHLPR	P43213	Pollen Allergen Phl p 1 [Precursor]	<i>Phleum pratense</i> (Common timothy)	138
Phl p 2	MPP2_PHLPR	P43214	Pollen Allergen Phl p 2 [Precursor]	<i>Phleum pratense</i> (Common timothy)	139
Phl p 5	MP5A_PHLPR	Q40962	Pollen Allergen Phl p 5a [Fragment]	<i>Phleum pratense</i> (Common timothy)	140
Phl p 5	MP5B_PHLPR	Q40963	Pollen Allergen Phl p 5b [Precursor] [Fragment]	<i>Phleum pratense</i> (Common timothy)	141
Phl p 6	MPP6_PHLPR	P43215	Pollen Allergen Phl p 6 [Precursor]	<i>Phleum pratense</i> (Common timothy)	1412
Phl p 11	PRO1_PHLPR	P35079	Profilin 1	<i>Phleum pratense</i> (Common timothy)	143
Phl p 11	PRO2_PHLPR	O24650	Profilin 2/4	<i>Phleum pratense</i> (Common timothy)	144
Phl p 11	PRO3_PHLPR	O24282	Profilin 3	<i>Phleum pratense</i> (Common timothy)	145
Poa p 9	MP91_POAPR	P22284	Pollen Allergen Kbg 31 [Precursor]	<i>Poa pratensis</i> (Kentucky bluegrass)	146
Poa p 9	MP92_POAPR	P22285	Pollen Allergen Kbg 41 [Precursor]	<i>Poa pratensis</i> (Kentucky bluegrass)	147
Poa p 9	MP93_POAPR	P22286	Pollen Allergen Kbg 60 [Precursor]	<i>Poa pratensis</i> (Kentucky bluegrass)	148
Pol a 5	VA5_POLAN	Q05109	Venom Allergen 5 [Precursor] [Fragment]	<i>Polistes annularis</i> (Paper wasp)	149
Pol d 5	VA5_POLDO	P81656	Venom Allergen 5	<i>Polistes dominulus</i> (European paper wasp)	150
Pol e 5	VA5_POLEX	P35759	Venom Allergen 5	<i>Polistes exclamans</i> (Paper wasp)	151
Pol f 5	VA5_POLFU	P35780	Venom Allergen 5	<i>Polistes fuscatus</i> (Paper wasp)	152
Pru a 1	PRU1_PRUAV	O24248	Major Allergen Pm a 1	<i>Prunus avium</i> (Cherry)	153
Rat n 1	MUP_RAT	P02761	Major Urinary Protein [Precursor]	<i>Rattus norvegicus</i> (Rat)	154
Sol i 2	VA2_SOLIN	P35775	Venom Allergen II [Precursor]	<i>Solenopsis invicta</i> (Red imported fire ant)	155
Sol i 3	VA3_SOLIN	P35778	Venom Allergen III	<i>Solenopsis invicta</i> (Red imported fire ant)	156
Sol i 4	VA4_SOLIN	P35777	Venom Allergen IV	<i>Solenopsis invicta</i> (Red imported fire ant)	157
Sol r 2	VA2SOLRI	P35776	Venom Allergen II	<i>Solenopsis richteri</i> (Black imported fire ant)	158
Sol r 3	VA3_SOLRI	P35779	Venom Allergen III	<i>Solenopsis richteri</i> (Black imported fire ant)	159
Ves c 5	VA51_VESCR	P35781	Venom Allergen 5.01	<i>Vespa crabro</i> (European hornet)	160
Ves c 5	VA52_VESCR	P35782	Venom Allergen 5.02	<i>Vespa crabro</i> (European hornet)	161
Ves f 5	VA5_VESFL	P35783	Venom Allergen 5	<i>Vespula flavopilosa</i> (Yellow jacket) (Wasp)	162
Ves g 5	VA5_VESGE	P35784	Venom Allergen 5	<i>Vespula germanica</i> (Yellow jacket) (Wasp)	163
Ves m 1	PA1_VESMC	P51528	Phospholipase A1	<i>Vespula maculifrons</i> (Eastern yellow jacket) (Wasp)	164
Ves m 5	VA5_VESMC	P35760	Venom Allergen 5	<i>Vespula maculifrons</i> (Eastern yellow jacket) (Wasp)	165
Ves p 5	VA5_VESPE	P35785	Venom Allergen 5	<i>Vespula pensylvanica</i> (Western yellow jacket) (Wasp)	166
Ves s 5	VA5_VESSQ	P35786	Venom Allergen 5	<i>Vespula squamosa</i> (Southern yellow jacket) (Wasp)	167
Ves v 1	PA1_VESVU	P49369	Phospholipase A1 [Precursor]	<i>Vespula vulgaris</i> (Yellow jacket) (Wasp)	168
Ves v 2	HUGA_VESVU	P49370	Hyaluronoglucosaminidase	<i>Vespula vulgaris</i> (Yellow jacket) (Wasp)	169
Ves v 5	VA5_VESVU	Q05110	Venom Allergen 5 [Precursor]	<i>Vespula vulgaris</i> (Yellow jacket) (Wasp)	170

TABLE 1-continued

Allergen	SWISS-PROT Entry	SWISS-PROT Accession No.	Protein Name	Source	SEQ ID NO.
Ves vi 5 I	VA5_VESV	P35787	Venom Allergen 5	<i>Vespula vidua</i> (Yellow jacket) (Wasp)	171
Vesp m 5	VA5_VESMA	P81657	Venom Allergen 5	<i>Vespa mandarinia</i> (Hornet)	172
Zea m 1	MPZ1_MAIZE	Q07154	Pollen Allergen Zea m 1	<i>Zea mays</i> (Maize)	173

Suitable vectors are prepared using standard techniques of recombinant DNA technology, and are, for example, described in "Molecular Cloning: A Laboratory Manual", 2nd edition (Sambrook et al., 1989); "Oligonucleotide Synthesis" (M. J. Gait, ed., 1984); "Animal Cell Culture" (R. I. Freshney, ed., 1987); "Methods in Enzymology" (Academic Press, Inc.); "Handbook of Experimental Immunology", 4th edition (D. M. Weir & C. C. Blackwell, eds., Blackwell Science Inc., 1987); "Gene Transfer Vectors for Mammalian Cells" (J. M. Miller & M. P. Calos, eds., 1987); "Current Protocols in Molecular Biology" (F. M. Ausubel et al., eds., 1987); "PCR: The Polymerase Chain Reaction", (Mullis et al., eds., 1994); and "Current Protocols in Immunology" (J. E. Coligan et al., eds., 1991). Isolated plasmids and DNA fragments are cleaved, tailored, and ligated together in a specific order to generate the desired vectors. After ligation, the vector containing the gene to be expressed is transformed into a suitable host cell.

Host cells can be any eukaryotic or prokaryotic hosts known for expression of heterologous proteins. Accordingly, the polypeptides of the present invention can be expressed in eukaryotic hosts, such as eukaryotic microbes (yeast) or cells isolated from multicellular organisms (mammalian cell cultures), plants and insect cells. Examples of mammalian cell lines suitable for the expression of heterologous polypeptides include monkey kidney CV1 cell line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney cell line 293S (Graham et al, *J. Gen. Virol.* 36:59 [1977]); baby hamster kidney cells (BHK, ATCC CCL 10); Chinese hamster ovary (CHO) cells (Urlaub and Chasin, *Proc. Natl. Acad. Sci. USA* 77:4216 [1980]); monkey kidney cells (CV1-76, ATCC CCL 70); African green monkey cells (VERO-76, ATCC CRL-1587); human cervical carcinoma cells (HELA, ATCC CCL 2); canine kidney cells (MDCK, ATCC CCL 34); human lung cells (W138, ATCC CCL 75); and human liver cells (Hep G2, HB 8065). In general myeloma cells, in particular those not producing any endogenous antibody, e.g. the non-immunoglobulin producing myeloma cell line SP2/0, are preferred for the production of the fusion molecules herein.

Eukaryotic expression systems employing insect cell hosts may rely on either plasmid or baculoviral expression systems. The typical insect host cells are derived from the fall army worm (*Spodoptera frugiperda*). For expression of a foreign protein these cells are infected with a recombinant form of the baculovirus *Autographa californica* nuclear polyhedrosis virus which has the gene of interest expressed under the control of the viral polyhedrin promoter. Other insects infected by this virus include a cell line known commercially as "High 5" (Invitrogen) which is derived from the cabbage looper (*Trichoplusia ni*). Another baculovirus sometimes used is the *Bombyx mori* nuclear polyhedrosis virus which infect the silk worm (*Bombyx mori*). Numerous baculovirus expression systems are commercially available, for example,

from Invitrogen (Bac-N-Blue™), Clontech (BacPAK™ Baculovirus Expression System), Life Technologies (BAC-TO-BAC™), Novagen (Bac Vector System™), Pharmingen and Quantum Biotechnologies). Another insect cell host is common fruit fly, *Drosophila melanogaster*, for which a transient or stable plasmid based transfection kit is offered commercially by Invitrogen (The DEST™ System).

Saccharomyces cerevisiae is the most commonly used among lower eukaryotic hosts. However, a number of other genera, species, and strains are also available and useful herein, such as *Pichia pastoris* (EP 183,070; Sreekrishna et al., *J. Basic Microbiol.* 28:165-278 (1988)). Yeast expression systems are commercially available, and can be purchased, for example, from Invitrogen (San Diego, Calif.). Other yeasts suitable for bi-functional protein expression include, without limitation, *Kluyveromyces* hosts (U.S. Pat. No. 4,943, 529), e.g. *Kluyveromyces lactis*; *Schizosaccharomyces pombe* (Beach and Nurse, *Nature* 290:140 (1981); *Aspergillus* hosts, e.g. *A. niger* (Kelly and Hynes, *EMBO J.* 4:475-479 (1985)) and *A. nidulans* (Ballance et al., *Biochem. Biophys. Res. Commun.* 112:284-289 (1983)), and *Hansenula* hosts, e.g. *Hansenula polymorpha*. Yeasts rapidly growth on inexpensive (minimal) media, the recombinant can be easily selected by complementation, expressed proteins can be specifically engineered for cytoplasmic localization or for extracellular export, and are well suited for large-scale fermentation.

Prokaryotes are the preferred hosts for the initial cloning steps, and are particularly useful for rapid production of large amounts of DNA, for production of single-stranded DNA templates used for site-directed mutagenesis, for screening many mutants simultaneously, and for DNA sequencing of the mutants generated. *E. coli* strains suitable for the production of the peptides of the present invention include, for example, BL21 carrying an inducible T7 RNA polymerase gene (Studier et al., *Methods Enzymol.* 185:60-98 (1990)); AD494 (DE3); EB105; and CB (*E. coli* B) and their derivatives; K12 strain 214 (ATCC 31,446); W3110 (ATCC 27,325); X1776 (ATCC 31,537); HB101 (ATCC 33,694); JM101 (ATCC 33,876); NM522 (ATCC 47,000); NM538 (ATCC 35,638); NM539 (ATCC 35,639), etc. Many other species and genera of prokaryotes may be used as well. Indeed, the peptides of the present invention can be readily produced in large amounts by utilizing recombinant protein expression in bacteria, where the peptide is fused to a cleavable ligand used for affinity purification.

Suitable promoters, vectors and other components for expression in various host cells are well known in the art and are disclosed, for example, in the textbooks listed above.

Whether a particular cell or cell line is suitable for the production of the polypeptides herein in a functionally active form, can be determined by empirical analysis. For example, an expression construct comprising the coding sequence of

the desired molecule may be used to transfect a candidate cell line. The transfected cells are then grown in culture, the medium collected, and assayed for the presence of secreted polypeptide. The product can then be quantitated by methods known in the art, such as by ELISA with an antibody specifically binding the IgG, IgE, or allergen portion of the molecule.

In certain instances, especially if the two polypeptide sequences making up the bifunctional molecule of the present invention are connected with a non-polypeptide linker, it may be advantageous to individually synthesize the first and second polypeptide sequences, e.g. by any of the recombinant approaches discussed above, followed by functionally linking the two sequences.

Alternatively, the two polypeptide sequences, or the entire molecule, may be prepared by chemical synthesis, such as solid phase peptide synthesis. Such methods are well known to those skilled in the art. In general, these methods employ either solid or solution phase synthesis methods, described in basic textbooks, such as, for example, J. M. Stewart and J. D. Young, *Solid Phase Peptide Synthesis*, 2nd Ed., Pierce Chemical Co., Rockford, Ill. (1984) and G. Barany and R. B. Merrifield, *The Peptide: Analysis Synthesis, Biology*, editors E. Gross and J. Meienhofer, Vol. 2, Academic Press, New York, (1980), pp. 3-254, for solid phase peptide synthesis techniques; and M. Bodansky, *Principles of Peptide Synthesis*, Springer-Verlag, Berlin (1984) and E. Gross and J. Meienhofer, Eds., *The Peptides: Analysis, Synthesis, Biology*, supra, Vol. 1, for classical solution synthesis.

The fusion molecules of the present invention may include amino acid sequence variants of native immunoglobulin (e.g. IgG and/or IgE) or allergen (e.g., Ara h 2 sequences). Such amino acid sequence variants can be produced by expressing the underlying DNA sequence in a suitable recombinant host cell, or by in vitro synthesis of the desired polypeptide, as discussed above. The nucleic acid sequence encoding a polypeptide variant is preferably prepared by site-directed mutagenesis of the nucleic acid sequence encoding the corresponding native (e.g. human) polypeptide. Particularly preferred is site-directed mutagenesis using polymerase chain reaction (PCR) amplification (see, for example, U.S. Pat. No. 4,683,195 issued 28 Jul. 1987; and *Current Protocols In Molecular Biology*, Chapter 15 (Ausubel et al., ed., 1991)). Other site-directed mutagenesis techniques are also well known in the art and are described, for example, in the following publications: *Current Protocols In Molecular Biology*, supra, Chapter 8; *Molecular Cloning: A Laboratory Manual*, 2nd edition (Sambrook et al., 1989); Zoller et al., *Methods Enzymol.* 100:468-500 (1983); Zoller & Smith, *DNA* 3:479-488 (1984); Zoller et al., *Nucl. Acids Res.*, 10:6487 (1987); Brake et al., *Proc. Natl. Acad. Sci. USA* 81:4642-4646 (1984); Botstein et al., *Science* 229:1193 (1985); Kunkel et al., *Methods Enzymol.* 154:367-82 (1987); Adelman et al., *DNA* 2:183 (1983); and Carter et al., *Nucl. Acids Res.*, 13:4331 (1986). Cassette mutagenesis (Wells et al., *Gene*, 34:315 [1985]), and restriction selection mutagenesis (Wells et al., *Philos. Trans. R. Soc. London SerA*, 317:415 [1986]) may also be used.

Amino acid sequence variants with more than one amino acid substitution may be generated in one of several ways. If the amino acids are located close together in the polypeptide chain, they may be mutated simultaneously, using one oligonucleotide that codes for all of the desired amino acid substitutions. If, however, the amino acids are located some distance from one another (e.g. separated by more than ten amino acids), it is more difficult to generate a single oligonucleotide that encodes all of the desired changes. Instead,

one of two alternative methods may be employed. In the first method, a separate oligonucleotide is generated for each amino acid to be substituted. The oligonucleotides are then annealed to the single-stranded template DNA simultaneously, and the second strand of DNA that is synthesized from the template will encode all of the desired amino acid substitutions. The alternative method involves two or more rounds of mutagenesis to produce the desired mutant.

The polypeptides of the invention can also be prepared by the combinatorial peptide library method disclosed, for example, in International Patent Publication PCT WO 92/09300. This method is particularly suitable for preparing and analyzing a plurality of molecules, that are variants of a given predetermined sequence, and is, therefore, particularly useful in identifying polypeptides with improved biological properties, which can then be produced by any technique known in the art, including recombinant DNA technology and/or chemical synthesis.

3. Therapeutic Uses of the Fusion Molecules of the Invention

The present invention provides a new therapeutic strategy for treating immediate hypersensitivity diseases mediated through the high-affinity IgE receptor. In particular, the invention provides compounds for use in the treatment of both allergic diseases where IgE bridging of FcεR receptors occurs and autoimmune disorders where autoantibodies bind to the FcεR.

Nature of the diseases targeted Following the Gell and Coombs Classification, allergic reactions are classified depending on the type of immune response induced and the resulting tissue damage that develops as a result of reactivity to an antigen. A Type I reaction (immediate hypersensitivity) occurs when an antigen (called an allergen in this case) entering the body encounters mast cells or basophils which are sensitized as a result of IgE to that antigen being attached to its high-affinity receptor, FcεRI. Upon reaching the sensitized mast cell, the allergen cross-links IgE bound to FcεRI, causing an increase in intracellular calcium (Ca²⁺) that triggers the release of pre-formed mediators, such as histamine and proteases, and newly synthesized, lipid-derived mediators such as leukotrienes and prostaglandins. These autocooids produce the acute clinical symptoms of allergy. The stimulated basophils and mast cells will also produce and release proinflammatory mediators, which participate in the acute and delayed phase of allergic reactions.

As discussed before and shown in Table 1 above, a large variety of allergens has been identified so far, and new allergens are identified, cloned and sequenced practically every day.

Ingestion of an allergen results in gastrointestinal and systemic allergic reactions. The most common food allergens involved are peanuts, shellfish, milk, fish, soy, wheat, egg and tree nuts such as walnuts. In susceptible people, these foods can trigger a variety of allergic symptoms, such as nausea, vomiting, diarrhea, urticaria, angioedema, asthma and full-blown anaphylaxis.

Inhalation of airborne allergens results in allergic rhinitis and allergic asthma, which can be acute or chronic depending on the nature of the exposure(s). Exposure to airborne allergens in the eye results in allergic conjunctivitis. Common airborne allergens include pollens, mold spores, dust mites and other insect proteins. Grass and weed and tree pollens are the most common cause of seasonal hay fever and allergic asthma.

Cutaneous exposure to an allergen, e.g. natural rubber latex proteins as found in latex gloves, may result in local allergic reactions manifest as hives (urticaria) at the places of contact with the allergen.

Systemic exposure to an allergen such as occurs with a bee sting, the injection of penicillin, or the use of natural rubber latex (NRL) gloves inside a patient during surgery may result in, cutaneous, gastrointestinal and respiratory reactions up to and including airway obstruction and full blown anaphylaxis. Hymenoptera stings are insects that commonly cause allergic reactions, often leading the anaphylactic shock. Examples include various bees including honeybees, yellow jackets, yellow hornets, wasps and white-faced hornets. Certain ants known as fire ants (*Solenopsis invicta*) are an increasing cause of allergy in the US as they expand their range in this country. Proteins in NRL gloves have become an increasing concern to health care workers and patients and at present, there is no successful form of therapy for this problem except avoidance.

Uses of compounds for targeted diseases The compounds disclosed herein can be used to acute or chronically inhibit IgE mediated reaction to major environmental and occupational allergens, can be used to provide for allergy vaccination (immunotherapy) to induce a state of non-allergic reactivity to specific allergens and can also have a prophylactic effect against allergic disease by preventing allergic sensitization to environmental and occupational allergens when administered to at-risk individuals (e.g., those at genetic risk of asthma and those exposed to occupational allergens in the workplace).

The bifunctional gamma-epsilon compounds described can be used to prevent allergic reactions to any specific allergen or group of allergens. By occupying a critical number of FcεRI receptors, these molecules will inhibit the ability of basophils and mast cells to react to any allergen so as to prevent including, without limitation, asthma, allergic rhinitis, atopic dermatitis, food allergies, urticaria and angioedema, up to and including anaphylactic shock. Thus these compounds could be used acutely to desensitize a patient so that the administration of a therapeutic agent (e.g. penicillin) can be given safely. Similarly, they can be used to desensitize a patient so that standard allergen vaccination may be given with greater safety, e.g. peanut or latex treatment. They can also be used as chronic therapy to prevent clinical reactivity to prevent environmental allergens such as foods or inhalant allergens.

The present invention as gamma allergen bifunctional fusion molecules provides for a novel form of allergy vaccination that will be safer and more effective the treatment of a varieties of IgE mediated allergic reactivity, including, without limitation, asthma, allergic rhinitis, atopic dermatitis, food allergies, urticaria and angioedema, up to and including anaphylactic shock. Having the allergen fused to a molecule that will bind to FcγRIIb on mast cells basophils will prevent the allergen being able to induce local or systemic allergic reactions. Such local or systemic allergic reactions are major problem in allergen vaccination as currently practiced. The gamma-allergen fusion proteins will be able to be given in higher doses over a shorter interval and with greater safety than standard allergen therapy. In addition, use of the gamma-allergen compounds will cause antigen specific desensitization to that specific allergen. Thus the gamma-allergen compounds will give a window of safe exposure to the allergen be it as an acute or recurring treatment as would be needed in using a therapeutic monoclonal antibody to which a patient has developed an allergic (IgE) response or as chronic treatment for prevention of unintentional exposures such as occurs with peanut allergens. This use is expected gain added importance, as the number of recombinant biological products

entering the clinical arena will be increasing dramatically in the near future. The gamma-allergen compounds can even be used along with conventional allergen vaccination so as to provide an extra margin of safety while large doses of standard allergen are given.

In addition, the chimeric gamma-epsilon compounds herein hold great promise for the treatment of chronic urticaria and angioedema. Urticaria is a skin symptom that may accompany allergies but often is idiopathic. It is a relatively common disorder caused by localized cutaneous mast cell degranulation, with resultant increased dermal vascular permeability culminating in pruritic wheals. Angioedema is a vascular reaction involving the deep dermis or subcutaneous or submucosal tissues caused by localized mast cell degranulation. This results in tissue swelling that is pruritic or painful. Chronic urticaria and angioedema often occur together although they occur individually as well. These conditions are common and once present for more than six months, they often last a decade or more. Although not fatal, they are very troubling to patients as the frequent recurring attaching disrupt daily activities and thereby result in significant morbidity. Standard therapy is often unsuccessful in these conditions and they are distressing to the point that chemotherapy with cyclosporine and other potent immunosuppressive drugs has recently been advocated. Increasing evidence suggests that as many as 60% of patients with these conditions actually have an autoimmune disease, in which they make functional antibodies against the FcεRI receptor. For further details, see Hide et al., *N. Engl. J. Med.* 328:1599-1604 (1993); Fiebiger et al., *J. Clin. Invest.* 96:2606-12 (1995); Fiebiger et al., *J. Clin. Invest.* 101:243-51 (1998); Kaplan, A. P., Urticaria and Angioedema, In: *Inflammation: Basic Principles and Clinical Correlates* (Galliin and Snyderman eds.), 3rd Edition, Lippincott & Wilkins, Philadelphia, 1999, pp. 915-928. The fusion molecules of the present invention are believed to form the basis for a novel and effective treatment of these diseases by safely blocking access to the FcεRI.

For therapeutic uses, including prevention, the compounds of the invention can be formulated as pharmaceutical compositions in admixture with pharmaceutically acceptable carriers or diluents. Methods for making pharmaceutical formulations are well known in the art. Techniques and formulations generally may be found in *Remington's Pharmaceutical Sciences*, 18th Edition, Mack Publishing Co., Easton, Pa. 1990. See, also, Wang and Hanson "Parenteral Formulations of Proteins and Peptides: Stability and Stabilizers", *Journal of Parenteral Science and Technology*, Technical Report No. 10, Supp. 42-2S (1988). A suitable administration format can best be determined by a medical practitioner for each patient individually.

Pharmaceutical compositions of the present invention can comprise a fusion molecule of the present invention along with conventional carriers and optionally other ingredients.

Suitable forms, in part, depend upon the use or the route of entry, for example oral, transdermal, inhalation, or by injection. Such forms should allow the agent or composition to reach a target cell whether the target cell is present in a multicellular host or in culture. For example, pharmacological agents or compositions injected into the blood stream should be soluble. Other factors are known in the art, and include considerations such as toxicity and forms that prevent the agent or composition from exerting its effect.

Carriers or excipients can also be used to facilitate administration of the compound. Examples of carriers and excipients include calcium carbonate, calcium phosphate, various sugars such as lactose, glucose, or sucrose, or types of starch, cellulose derivatives, gelatin, vegetable oils, polyethylene

glycols and physiologically compatible solvents. The compositions or pharmaceutical composition can be administered by different routes including, but not limited to, oral, intravenous, intra-arterial, intraperitoneal, subcutaneous, intranasal or intrapulmonary routes.

The desired isotonicity of the compositions can be accomplished using sodium chloride or other pharmaceutically acceptable agents such as dextrose, boric acid, sodium tartrate, propylene glycol, polyols (such as mannitol and sorbitol), or other inorganic or organic solutes.

For systemic administration, injection is preferred, e.g., intramuscular, intravenous, intra-arterial, etc. For injection, the compounds of the invention are formulated in liquid solutions, preferably in physiologically compatible buffers such as Hank's solution or Ringer's solution. Alternatively, the compounds of the invention are formulated in one or more excipients (e.g., propylene glycol) that are generally accepted as safe as defined by USP standards. They can, for example, be suspended in an inert oil, suitably a vegetable oil such as sesame, peanut, olive oil, or other acceptable carrier. Preferably, they are suspended in an aqueous carrier, for example, in an isotonic buffer solution at pH of about 5.6 to 7.4. These compositions can be sterilized by conventional sterilization techniques, or can be sterile filtered. The compositions can contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions, such as pH buffering agents. Useful buffers include for example, sodium acetate/acetic acid buffers. A form of repository or "depot" slow release preparation can be used so that therapeutically effective amounts of the preparation are delivered into the bloodstream over many hours or days following transdermal injection or delivery. In addition, the compounds can be formulated in solid form and redissolved or suspended immediately prior to use. Lyophilized forms are also included.

Alternatively, certain molecules identified in accordance with the present invention can be administered orally. For oral administration, the compounds are formulated into conventional oral dosage forms such as capsules, tablets and tonics.

Systemic administration can also be by transmucosal or transdermal. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, bile salts and fusidic acid derivatives. In addition, detergents can be used to facilitate permeation. Transmucosal administration can be, for example, through nasal sprays or using suppositories.

A preferred route for administration of the compounds of the invention may be inhalation for intranasal and/or intrapulmonary delivery. For administration by inhalation, usually inhalable dry power compositions or aerosol compositions are used, where the size of the particles or droplets is selected to ensure deposition of the active ingredient in the desired part of the respiratory tract, e.g. throat, upper respiratory tract or lungs. Inhalable compositions and devices for their administration are well known in the art. For example, devices for the delivery of aerosol medications for inspiration are known. One such device is a metered dose inhaler that delivers the same dosage of medication to the patient upon each actuation of the device. Metered dose inhalers typically include a canister containing a reservoir of medication and propellant under pressure and a fixed volume metered dose chamber. The canister is inserted into a receptacle in a body or base having a mouthpiece or nosepiece for delivering medication to the patient. The patient uses the device by manually pressing the canister into the body to close a filling valve and capture a metered dose of medication inside the chamber and

to open a release valve which releases the captured, fixed volume of medication in the dose chamber to the atmosphere as an aerosol mist. Simultaneously, the patient inhales through the mouthpiece to entrain the mist into the airway.

5 The patient then releases the canister so that the release valve closes and the filling valve opens to refill the dose chamber for the next administration of medication. See, for example, U.S. Pat. No. 4,896,832 and a product available from 3M Healthcare known as Aerosol Sheathed Actuator and Cap.

10 Another device is the breath actuated metered dose inhaler that operates to provide automatically a metered dose in response to the patient's inspiratory effort. One style of breath actuated device releases a dose when the inspiratory effort moves a mechanical lever to trigger the release valve. Another style releases the dose when the detected flow rises above a preset threshold, as detected by a hot wire anemometer. See, for example, U.S. Pat. Nos. 3,187,748; 3,565,070; 3,814,297; 3,826,413; 4,592,348; 4,648,393; 4,803,978.

15 Devices also exist to deliver dry powdered drugs to the patient's airways (see, e.g. U.S. Pat. No. 4,527,769) and to deliver an aerosol by heating a solid aerosol precursor material (see, e.g. U.S. Pat. No. 4,922,901). These devices typically operate to deliver the drug during the early stages of the patient's inspiration by relying on the patient's inspiratory flow to draw the drug out of the reservoir into the airway or to actuate a heating element to vaporize the solid aerosol precursor.

20 Devices for controlling particle size of an aerosol are also known, see, for example, U.S. Pat. Nos. 4,790,305; 4,926,852; 4,677,975; and 3,658,059.

For topical administration, the compounds of the invention are formulated into ointments, salves, gels, or creams, as is generally known in the art.

25 If desired, solutions of the above compositions can be thickened with a thickening agent such as methyl cellulose. They can be prepared in emulsified form, either water in oil or oil in water. Any of a wide variety of pharmaceutically acceptable emulsifying agents can be employed including, for example, acacia powder, a non-ionic surfactant (such as a Tween), or an ionic surfactant (such as alkali polyether alcohol sulfates or sulfonates, e.g., a Triton).

30 Compositions useful in the invention are prepared by mixing the ingredients following generally accepted procedures. For example, the selected components can be mixed simply in a blender or other standard device to produce a concentrated mixture which can then be adjusted to the final concentration and viscosity by the addition of water or thickening agent and possibly a buffer to control pH or an additional solute to control tonicity.

35 The amounts of various compounds for use in the methods of the invention to be administered can be determined by standard procedures. Generally, a therapeutically effective amount is between about 100 mg/kg and 10^{-12} mg/kg depending on the age and size of the patient, and the disease or disorder associated with the patient. Generally, it is an amount between about 0.05 and 50 mg/kg, more preferably between about 1.0 and 10 mg/kg for the individual to be treated. The determination of the actual dose is well within the skill of an ordinary physician.

40 The compounds of the present invention may be administered in combination with one or more further therapeutic agent for the treatment of IgE-mediated allergic diseases or conditions. Such further therapeutic agents include, without limitation, corticosteroids, β -antagonists, theophylline, leukotriene inhibitors, allergen vaccination, soluble recombinant human soluble IL-4 receptors (Immunogen), anti-IL-4 monoclonal antibodies (Protein Design Labs), and anti-IgE

antibodies, such as the recombinant human anti-IgE monoclonal antibody rhuMAb-E25 (Genentech, Inc.) which is currently in advanced clinical trials for the treatment of patients with atopic asthma, and other allergic diseases, such as allergic rhinitis and atopic dermatitis (see, e.g. Barnes, *The New England Journal of Medicine* 341:2006-2008 (1999)). Thus the compounds of the present invention can be used to supplement traditional allergy therapy, such as corticosteroid therapy performed with inhaled or oral corticosteroids.

4. Articles of Manufacture

The invention also provides articles of manufacture comprising the single-chain fusion compounds herein. The article of manufacture comprises a container and a label or package insert on or associated with the container. Suitable containers include, for example, bottles, vials, syringes, etc. The containers may be formed from a variety of materials such as glass or plastic. The container holds a composition which is effective for treating the condition and may have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). The container may also be an inhalation device such as those discussed above. At least one active agent in the composition is a fusion compound of the invention. The label or package insert indicates that the composition is used for treating the condition of choice, such as an allergic condition, e.g. asthma or any of the IgE-mediated allergies discussed above. The article of manufacture may further comprise a further container comprising a pharmaceutically-acceptable buffer, such as bacteriostatic water for injection (BWFI), phosphate-buffered saline, Ringer's solution and dextrose solution. It may further include other materials desirable from a commercial and user standpoint, including other buffers, diluents, filters, needles, and syringes.

Further details of the invention are illustrated by the following non-limiting Example.

Example

Construction and Expression of a Chimeric Human Fc γ -Fc ϵ Fusion Protein

Materials and Methods

Plasmids, vectors and cells—Plasmid pAG 4447 containing genomic DNA encoding human IgE constant region and expression vector pAN 1872 containing human genomic DNA encoding the hinge-CH2-CH3 portion of IgG₁ constant region were obtained from the laboratory of Dr. Morrison. pAN 1872 is derived from the pDisplay vector (Invitrogen). pAG 4447 was developed and used as a cloning intermediate in the construction of a human IgE expression vector disclosed in *J. Biol. Chem.* 271:3428-3436 (1996). To construct the chimeric gene, a pair of primers were designed to amplify the human IgE constant region (CH2-CH3-CH4). 5'-end primer:

5' GCTCGAGGGTGGAGGCGGTTTCAGGCGGAGGTGGCTCTGGCGGTGGCG
GATCGTTCACCCCGCCACCGTGAAG3', (SEQ ID NO: 174)

containing a flexible linker sequence and an XhoI site.

3' end primer:

5' GGCGGCCGCTCATTACCGGGATTACAGACAC3',
(SEQ ID NO: 175)

containing an NotI.

After amplification, the PCR products were cloned into pCR2.1 vector (Invitrogen). The sequences of the products were confirmed. Then, the ZhoI-NotI fragment was inserted into the 1782 pAN vector, following the IgG₁ CH3 domain in the same reading frame by a (Gly₄Ser)₃ flexible linker. SP2.0 murine myeloma cell line was selected as host for expression because it does not secrete any antibody.

Expression and Purification—The expression vector containing chimeric Fc γ -Fc ϵ gene was linearized at the PcuI site and transfected into SP2/0 cells by electroporation (Bio-Rad). Stable transfectants were selected for growth in medium containing 1 mg/ml geneticine. Clones producing the fusion protein were identified by ELISA using plates coating anti-human IgE (CIA7.12) or IgG (Sigma) antibody. Supernatants from clones were added to wells, and bound protein was detected using goat anti-human IgE or IgG conjugated to alkaline phosphatase (KPL). The fusion protein was purified from the supernatants and ascites by using rProtein A column (Pharmacia).

Western Blotting—The purified protein was run on 7.5% SDS polyacrylamide gel. After transfer, the nylon membrane was blocked by 4% bovine serum albumin/PBS/Tween overnight at 4° C. For protein detection, the blot was probed with either goat anti-human IgE (ϵ chain specific) or goat anti-human IgG (γ chain-specific) conjugated to alkaline phosphatase (KPL). Color development was performed with an alkaline phosphatase conjugated substrate kit (Bio-Rad).

Binding Test—In order to confirm the binding, Fc ϵ RI transfected cells (CHO 3D10) or human HMC-1 cells that express Fc γ RIIb but not Fc ϵ RI were stained with purified fusion protein and then analyzed by flow cytometry. Briefly, cells were collected and washed. The cells were then incubated with 5 μ l of 1 mg/ml GE2, PS IgE or human IgG at 4° C. for 60 minutes. After two washes, the cells were stained with FITC conjugated anti-human IgE or IgG at 4° C. for 60 minutes, and visualized by flow cytometry.

Inhibition of Basophil Histamine Release—Acid-stripped Percoll-enriched human blood basophils were primed with 1-10 μ g/ml of chimeric human anti-NP IgE at 37° C. in a 5% CO₂ incubator and one hour later, challenged with 30 ng of NP-BSA (Kepley, J. *Allergy Clin. Immunol.* 106:337-348 (2000)). Histamine release was measured in the supernatants 30 minutes later. GE2 or control human myeloma IgE was added at various doses and times to test the effects on histamine release.

Passive Cutaneous Anaphylaxis Model—Transgenic mice expressing the human Fc ϵ R1a chain and with the murine Fc ϵ R1 α chain knocked out (provided by Dr. Jean-Pierre Kinet, Harvard Medical School, Boston, Mass., Dombrowicz, et al, *J. Immunol.* 157:1645-1654. (1996)) were primed cutaneously with either recombinant human anti-dansyl or anti-NP IgE. Individual sites were then injected with saline, GE2 or IgE myeloma protein. Four hours later, mice were given a systemic challenge with dansyl-OVA or NP-BSA plus Evans blue, and the resulting area of reaction was measured.

Results

Western blotting showed that the chimeric protein (designated GE2) was expressed as the predicted dimer of approximately 140 kD. The GE2 protein reacted with both anti-human ϵ and anti-human γ chain-specific antibodies.

GE2 showed the ability to inhibit IgE-mediated release of histamine from fresh human basophils. The results of the dose-dependent inhibition of basophil histamine release using the fusion protein GE2 (\pm SEM; n+3 separate donors, each in duplicate) are shown in FIG. 8. The data show that, when added to fresh human basophils along with the sensitizing anti-NP IgE antibody, GE2 inhibited subsequent NP-induced release of histamine in a dose-dependent manner, more effectively than an equivalent amount of native human IgE protein. This was time dependent as expected with the greatest effect being observed when the GE2 was added with the sensitizing anti-NP IgE antibody. No effect was observed if the GE2 was given simultaneously with the antigen challenge.

To test the in vivo function of GE2, the transgenic passive cutaneous anaphylaxis described above was used. The results are shown in FIG. 9. The size and color of the reaction at the sites of GE2 injection were decreased compared to those

injected with comparable amount of human IgE. These results demonstrate that the GE2 protein is able to inhibit mast cell/basophil function greater than an equivalent amount of IgE and implicates binding to both Fc ϵ RI and FC γ R.

Analysis of binding using flow cytometry showed that the GE2 protein bound in a fashion similar to native IgE to the human Fc γ RII expressed on HMC-1 cells. The data are shown in FIG. 10. Similar results were obtained for the Fc ϵ RI on 3D10 cells, as shown in FIG. 11.

All references cited throughout the specification are hereby expressly incorporated by reference. It is understood that the application of the teachings of the present invention to a specific problem or situation will be within the capabilities of one having ordinary skill in the art in light of the teachings contained herein. Examples of the products of the present invention and representative processes for their production and use should not be construed to limit the invention.

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 177

<210> SEQ ID NO 1

<211> LENGTH: 696

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 1

```

gagcccaaat cttgtgacaa aactcacaca tgcccaccgt gccagcacc tgaactcctg      60
gggggaccgt cagtcttctt cttcccccca aaacccaagg acaccctcat gatctcccgg      120
accctgagg tcacatgctt ggtggtggac gtgagccacg aagaccctga ggtcaagtcc      180
aactggtacg tggacggcgt ggagggtgcat aatgttaaga caaagccgcg ggaggagcag      240
tacaacagca cgtaccgtgt ggtcagcgtc ctcaccgtcc tgcaccagaa ctggatgaat      300
ggaaaggagt acaagtgcaa ggtctccaac aaagccctcc cagcccccat cgagaaaacc      360
atctccaaag ccaaagtgca gccccgagaa ccacaggtgt acaccctgcc cccatcccgg      420
gatgagctga ccaagaacca ggtcagcctg acctgcctgg tcaaaggctt ctatcccagc      480
gacatcgccg tggagtggga gagcaatggg cagccggaga acaactaaa gaccacgcct      540
cccgtgctgg actccgtcgg ctcttctctt ctctacagca agctcacctg ggacaagagc      600
agggtggcagc aggggaactt cttctcatgc tccgtgatgc atgaggctct gcacaaccac      660
taccagcaga ggagcctctc cctgtctccg ggtaaa                                696

```

<210> SEQ ID NO 2

<211> LENGTH: 330

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 2

```

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
 1           5           10          15
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
 20          25          30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
 35          40          45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
 50          55          60

```


-continued

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
 65 70 75 80
 Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
 85 90 95
 Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
 100 105 110
 Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
 115 120 125
 Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
 130 135 140
 Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
 145 150 155 160
 Tyr Val Asp Gly Val Glu Val His Asn Val Lys Thr Lys Pro Arg Glu
 165 170 175
 Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
 180 185 190
 His Gln Asn Trp Met Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
 195 200 205
 Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Val
 210 215 220
 Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
 225 230 235 240
 Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
 245 250 255
 Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
 260 265 270
 Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Val Gly Ser Phe Phe
 275 280 285
 Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
 290 295 300
 Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Gln
 305 310 315 320
 Gln Arg Ser Leu Ser Leu Ser Pro Gly Lys
 325 330

<210> SEQ ID NO 3
 <211> LENGTH: 232
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
 1 5 10 15
 Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
 20 25 30
 Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
 35 40 45
 Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
 50 55 60
 Asp Gly Val Glu Val His Asn Val Lys Thr Lys Pro Arg Glu Glu Gln
 65 70 75 80
 Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
 85 90 95
 Asn Trp Met Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala

-continued

100	105	110
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Val Gln Pro 115 120 125		
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr 130 135 140		
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser 145 150 155 160		
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr 165 170 175		
Lys Thr Thr Pro Pro Val Leu Asp Ser Val Gly Ser Phe Phe Leu Tyr 180 185 190		
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe 195 200 205		
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Gln Gln Arg 210 215 220		
Ser Leu Ser Leu Ser Pro Gly Lys 225 230		

<210> SEQ ID NO 4
 <211> LENGTH: 1445
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 4

```

tccacacaga gccatccgt cttccccttg acccgctgct gcaaaaacat tccctccaat 60
gccacctcgg tgactctggg ctgcctggcc acgggctact tcccggagcc ggtgatggtg 120
acctgggaca caggctccct caacgggaca actatgacct taccagccac caccctcacg 180
ctctctggtc actatgccac catcagcttg ctgaccgtct cgggtgctg ggccaagcag 240
atgttcacct gccgtgtggc acacactcca tcgtccacag actgggtcga caacaaaacc 300
ttcagcgtct gctccaggga cttcaccccg cccaccgtga agatcttaca gtctcctgc 360
gacggcggcg ggcactccc cccgaccatc cagctcctgt gcctcgtctc tgggtacacc 420
ccagggacta tcaacatcac ctggctggag gacgggcagg tcatggacgt ggacttgctc 480
accgctctta ccacgcagga ggggtgagctg gcctccacac aaagcgagct caccctcagc 540
cagaagcact ggctgtcaga ccgcacctac acctgccagg tcacctatca aggtcacacc 600
tttgaggaca gcaccaagaa gtgtgcagat tccaaccoga gaggggtgag cgctaccta 660
agccggccca gcccgttcga cctgttcac cgaagtgc ccacgatcac ctgtctggtg 720
gtggacctgg caccagcaa ggggaccgtg aacctgacct ggteccgggc cagtgggaag 780
cctgtgaacc actccaccag aaaggaggag aagcagcgca atggcacgtt aaccgtcacg 840
tccaccctgc cgggtggcac ccgagactgg atcgaggggg agacctacca gtgcaggggtg 900
accaccccc acctgccag ggcctcatg cgggtccaga ccaagaccag cggcccgcgt 960
gtgccccgg aagtctatgc gtttgcgac cggagtggc cggggagccg ggacaagcgc 1020
accctgcct gcctgatcca gaacttcac cctgaggaca tctcgggtgca gtggctgcac 1080
aacgaggtgc agtcccga cggccggcac agcacgacgc agccccgaa gaccaagggc 1140
tccggttct tcgtcttcag ccgcctggag gtgaccaggg ccgaatggga gcagaaagat 1200
gagttcatct gccgtgcagt ccatgaggca gcgagccct cacagaccgt ccagcgagcg 1260
gtgtctgtaa atcccgtaa atgacgtact cctgcctccc tccctcccag ggctccatcc 1320
agctgtgcag tggggaggac tggccagacc ttctgtccac tggtgcaatg accccaggaa 1380

```


-continued

 gctacccccca ataaactgtg cctgctcaga gccccagtac acccattett gggagcgggc 1440

agggc 1445

<210> SEQ ID NO 5

<211> LENGTH: 427

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 5

 Ser Thr Gln Ser Pro Ser Val Phe Pro Leu Thr Arg Cys Cys Lys Asn
 1 5 10 15

 Ile Pro Ser Asn Ala Thr Ser Val Thr Leu Gly Cys Leu Ala Thr Gly
 20 25 30

 Tyr Phe Pro Glu Pro Val Met Val Thr Trp Asp Thr Gly Ser Leu Asn
 35 40 45

 Gly Thr Thr Met Thr Leu Pro Ala Thr Thr Leu Thr Leu Ser Gly His
 50 55 60

 Tyr Ala Thr Ile Ser Leu Leu Thr Val Ser Gly Ala Trp Ala Lys Gln
 65 70 75 80

 Met Phe Thr Cys Arg Val Ala His Thr Pro Ser Ser Thr Asp Trp Val
 85 90 95

 Asp Asn Lys Thr Phe Ser Val Cys Ser Arg Asp Phe Thr Pro Pro Thr
 100 105 110

 Val Lys Ile Leu Gln Ser Ser Cys Asp Gly Gly Gly His Phe Pro Pro
 115 120 125

 Thr Ile Gln Leu Leu Cys Leu Val Ser Gly Tyr Thr Pro Gly Thr Ile
 130 135 140

 Asn Ile Thr Trp Leu Glu Asp Gly Gln Val Met Asp Val Asp Leu Ser
 145 150 155 160

 Thr Ala Ser Thr Thr Gln Glu Gly Glu Leu Ala Ser Thr Gln Ser Glu
 165 170 175

 Leu Thr Leu Ser Gln Lys His Trp Leu Ser Asp Arg Thr Tyr Thr Cys
 180 185 190

 Gln Val Thr Tyr Gln Gly His Thr Phe Glu Asp Ser Thr Lys Lys Cys
 195 200 205

 Ala Asp Ser Asn Pro Arg Gly Val Ser Ala Tyr Leu Ser Arg Pro Ser
 210 215 220

 Pro Phe Asp Leu Phe Ile Arg Lys Ser Pro Thr Ile Thr Cys Leu Val
 225 230 235 240

 Val Asp Leu Ala Pro Ser Lys Gly Thr Val Asn Leu Thr Trp Ser Arg
 245 250 255

 Ala Ser Gly Lys Pro Val Asn His Ser Thr Arg Lys Glu Glu Lys Gln
 260 265 270

 Arg Asn Gly Thr Leu Thr Val Thr Ser Thr Leu Pro Val Gly Thr Arg
 275 280 285

 Asp Trp Ile Glu Gly Glu Thr Tyr Gln Cys Arg Val Thr His Pro His
 290 295 300

 Leu Pro Arg Ala Leu Met Arg Ser Thr Thr Lys Thr Ser Gly Pro Arg
 305 310 315 320

 Ala Ala Pro Glu Val Tyr Ala Phe Ala Thr Pro Glu Trp Pro Gly Ser
 325 330 335

 Arg Asp Lys Arg Thr Leu Ala Cys Leu Ile Gln Asn Phe Met Pro Glu
 340 345 350

-continued

Asp Ile Ser Val Gln Trp Leu His Asn Glu Val Gln Leu Pro Asp Ala
 355 360 365

Arg His Ser Thr Thr Gln Pro Arg Lys Thr Lys Gly Ser Gly Phe Phe
 370 375 380

Val Phe Ser Arg Leu Glu Val Thr Arg Ala Glu Trp Glu Gln Lys Asp
 385 390 395 400

Glu Phe Ile Cys Arg Ala Val His Glu Ala Ala Ser Pro Ser Gln Thr
 405 410 415

Val Gln Arg Ala Val Ser Val Asn Pro Gly Lys
 420 425

<210> SEQ ID NO 6
 <211> LENGTH: 320
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 6

Phe Thr Pro Pro Thr Val Lys Ile Leu Gln Ser Ser Cys Asp Gly Gly
 1 5 10 15

Gly His Phe Pro Pro Thr Ile Gln Leu Leu Cys Leu Val Ser Gly Tyr
 20 25 30

Thr Pro Gly Thr Ile Asn Ile Thr Trp Leu Glu Asp Gly Gln Val Met
 35 40 45

Asp Val Asp Leu Ser Thr Ala Ser Thr Thr Gln Glu Gly Glu Leu Ala
 50 55 60

Ser Thr Gln Ser Glu Leu Thr Leu Ser Gln Lys His Trp Leu Ser Asp
 65 70 75 80

Arg Thr Tyr Thr Cys Gln Val Thr Tyr Gln Gly His Thr Phe Glu Asp
 85 90 95

Ser Thr Lys Lys Cys Ala Asp Ser Asn Pro Arg Gly Val Ser Ala Tyr
 100 105 110

Leu Ser Arg Pro Ser Pro Phe Asp Leu Phe Ile Arg Lys Ser Pro Thr
 115 120 125

Ile Thr Cys Leu Val Val Asp Leu Ala Pro Ser Lys Gly Thr Val Asn
 130 135 140

Leu Thr Trp Ser Arg Ala Ser Gly Lys Pro Val Asn His Ser Thr Arg
 145 150 155 160

Lys Glu Glu Lys Gln Arg Asn Gly Thr Leu Thr Val Thr Ser Thr Leu
 165 170 175

Pro Val Gly Thr Arg Asp Trp Ile Glu Gly Glu Thr Tyr Gln Cys Arg
 180 185 190

Val Thr His Pro His Leu Pro Arg Ala Leu Met Arg Ser Thr Thr Lys
 195 200 205

Thr Ser Gly Pro Arg Ala Ala Pro Glu Val Tyr Ala Phe Ala Thr Pro
 210 215 220

Glu Trp Pro Gly Ser Arg Asp Lys Arg Thr Leu Ala Cys Leu Ile Gln
 225 230 235 240

Asn Phe Met Pro Glu Asp Ile Ser Val Gln Trp Leu His Asn Glu Val
 245 250 255

Gln Leu Pro Asp Ala Arg His Ser Thr Thr Gln Pro Arg Lys Thr Lys
 260 265 270

Gly Ser Gly Phe Phe Val Phe Ser Arg Leu Glu Val Thr Arg Ala Glu
 275 280 285

Trp Glu Gln Lys Asp Glu Phe Ile Cys Arg Ala Val His Glu Ala Ala
 290 295 300

-continued

Ser Pro Ser Gln Thr Val Gln Arg Ala Val Ser Val Asn Pro Gly Lys
305 310 315 320

<210> SEQ ID NO 7
<211> LENGTH: 569
<212> TYPE: PRT
<213> ORGANISM: Unknown
<220> FEATURE:
<223> OTHER INFORMATION: Fusion between hinge-CH2-CH3 (IgG1) to
CH2-CH3-CH4 (IgE)

<400> SEQUENCE: 7

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
20 25 30
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
35 40 45
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
50 55 60
Asp Gly Val Glu Val His Asn Val Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75 80
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
85 90 95
Asn Trp Met Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
100 105 110
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Val Gln Pro
115 120 125
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
130 135 140
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
145 150 155 160
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
165 170 175
Lys Thr Thr Pro Pro Val Leu Asp Ser Val Gly Ser Phe Phe Leu Tyr
180 185 190
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
195 200 205
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Gln Gln Arg
210 215 220
Ser Leu Ser Leu Ser Pro Gly Lys Val Glu Gly Gly Gly Gly Ser Gly
225 230 235 240
Gly Gly Gly Ser Gly Gly Gly Gly Ser Phe Thr Pro Pro Thr Val Lys
245 250 255
Ile Leu Gln Ser Ser Cys Asp Gly Gly Gly His Phe Pro Pro Thr Ile
260 265 270
Gln Leu Leu Cys Leu Val Ser Gly Tyr Thr Pro Gly Thr Ile Asn Ile
275 280 285
Thr Trp Leu Glu Asp Gly Gln Val Met Asp Val Asp Leu Ser Thr Ala
290 295 300
Ser Thr Thr Gln Glu Gly Glu Leu Ala Ser Thr Gln Ser Glu Leu Thr
305 310 315 320
Leu Ser Gln Lys His Trp Leu Ser Asp Arg Thr Tyr Thr Cys Gln Val
325 330 335
Thr Tyr Gln Gly His Thr Phe Glu Asp Ser Thr Lys Lys Cys Ala Asp

-continued

340					345					350					
Ser	Asn	Pro	Arg	Gly	Val	Ser	Ala	Tyr	Leu	Ser	Arg	Pro	Ser	Pro	Phe
		355					360					365			
Asp	Leu	Phe	Ile	Arg	Lys	Ser	Pro	Thr	Ile	Thr	Cys	Leu	Val	Val	Asp
	370					375					380				
Leu	Ala	Pro	Ser	Lys	Gly	Thr	Val	Asn	Leu	Thr	Trp	Ser	Arg	Ala	Ser
	385					390					395				400
Gly	Lys	Pro	Val	Asn	His	Ser	Thr	Arg	Lys	Glu	Glu	Lys	Gln	Arg	Asn
				405					410					415	
Gly	Thr	Leu	Thr	Val	Thr	Ser	Thr	Leu	Pro	Val	Gly	Thr	Arg	Asp	Trp
			420					425					430		
Ile	Glu	Gly	Glu	Thr	Tyr	Gln	Cys	Arg	Val	Thr	His	Pro	His	Leu	Pro
		435					440					445			
Arg	Ala	Leu	Met	Arg	Ser	Thr	Thr	Lys	Thr	Ser	Gly	Pro	Arg	Ala	Ala
	450					455					460				
Pro	Glu	Val	Tyr	Ala	Phe	Ala	Thr	Pro	Glu	Trp	Pro	Gly	Ser	Arg	Asp
	465					470					475				480
Lys	Arg	Thr	Leu	Ala	Cys	Leu	Ile	Gln	Asn	Phe	Met	Pro	Glu	Asp	Ile
				485					490					495	
Ser	Val	Gln	Trp	Leu	His	Asn	Glu	Val	Gln	Leu	Pro	Asp	Ala	Arg	His
			500						505				510		
Ser	Thr	Thr	Gln	Pro	Arg	Lys	Thr	Lys	Gly	Ser	Gly	Phe	Phe	Val	Phe
		515					520					525			
Ser	Arg	Leu	Glu	Val	Thr	Arg	Ala	Glu	Trp	Glu	Gln	Lys	Asp	Glu	Phe
	530					535					540				
Ile	Cys	Arg	Ala	Val	His	Glu	Ala	Ala	Ser	Pro	Ser	Gln	Thr	Val	Gln
	545					550					555				560
Arg	Ala	Val	Ser	Val	Asn	Pro	Gly	Lys							
				565											

<210> SEQ ID NO 8
 <211> LENGTH: 159
 <212> TYPE: PRT
 <213> ORGANISM: Alnus glutinosa (Alder)
 <220> FEATURE:

<400> SEQUENCE: 8

Gly	Val	Phe	Asn	Tyr	Glu	Ala	Glu	Thr	Pro	Ser	Val	Ile	Pro	Ala	Ala
1				5					10					15	
Arg	Leu	Phe	Lys	Ala	Phe	Ile	Leu	Asp	Gly	Asp	Lys	Leu	Leu	Pro	Lys
			20					25					30		
Val	Ala	Pro	Glu	Ala	Val	Ser	Ser	Val	Glu	Asn	Ile	Glu	Gly	Asn	Gly
		35					40					45			
Gly	Pro	Gly	Thr	Ile	Lys	Lys	Ile	Thr	Phe	Pro	Glu	Gly	Ser	Pro	Phe
	50					55					60				
Lys	Tyr	Val	Lys	Glu	Arg	Val	Asp	Glu	Val	Asp	Arg	Val	Asn	Phe	Lys
	65				70					75					80
Tyr	Ser	Phe	Ser	Val	Ile	Glu	Gly	Gly	Ala	Val	Gly	Asp	Ala	Leu	Glu
			85						90					95	
Lys	Val	Cys	Asn	Glu	Ile	Lys	Ile	Val	Ala	Ala	Pro	Asp	Gly	Gly	Ser
			100					105					110		
Ile	Leu	Lys	Ile	Ser	Asn	Lys	Phe	His	Thr	Lys	Gly	Asp	His	Glu	Ile
		115					120					125			
Asn	Ala	Glu	Gln	Ile	Lys	Ile	Glu	Lys	Glu	Lys	Ala	Val	Gly	Leu	Leu
						135					140				

-continued

Lys Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
 145 150 155

<210> SEQ ID NO 9
 <211> LENGTH: 113
 <212> TYPE: PRT
 <213> ORGANISM: *Alternaria alternata*

<400> SEQUENCE: 9

Met Lys His Leu Ala Ala Tyr Leu Leu Leu Gly Leu Gly Gly Asn Thr
 1 5 10 15
 Ser Pro Ser Ala Ala Asp Val Lys Ala Val Leu Glu Ser Val Gly Ile
 20 25 30
 Glu Ala Asp Ser Asp Arg Leu Asp Lys Leu Ile Ser Glu Leu Glu Gly
 35 40 45
 Lys Asp Ile Asn Glu Leu Ile Ala Ser Gly Ser Glu Lys Leu Ala Ser
 50 55 60
 Val Pro Ser Gly Gly Ala Gly Gly Ala Ala Ala Ser Gly Gly Ala Ala
 65 70 75 80
 Ala Ala Gly Gly Ser Ala Gln Ala Glu Ala Ala Pro Glu Ala Ala Lys
 85 90 95
 Glu Glu Glu Lys Glu Glu Ser Asp Glu Asp Met Gly Phe Gly Leu Phe
 100 105 110

Asp

<210> SEQ ID NO 10
 <211> LENGTH: 204
 <212> TYPE: PRT
 <213> ORGANISM: *Alternaria alternata*

<400> SEQUENCE: 10

Met Ala Pro Lys Ile Ala Ile Val Tyr Tyr Ser Met Tyr Gly His Ile
 1 5 10 15
 Lys Lys Met Ala Asp Ala Glu Leu Lys Gly Ile Gln Glu Ala Gly Gly
 20 25 30
 Asp Ala Lys Leu Phe Gln Val Ala Glu Thr Leu Pro Gln Glu Val Leu
 35 40 45
 Asp Lys Met Tyr Ala Pro Pro Lys Asp Ser Ser Val Pro Val Leu Glu
 50 55 60
 Asp Pro Ala Val Leu Glu Glu Phe Asp Gly Ile Leu Phe Gly Ile Pro
 65 70 75 80
 Thr Arg Tyr Gly Asn Phe Pro Ala Gln Phe Lys Thr Phe Trp Asp Lys
 85 90 95
 Thr Gly Lys Gln Trp Gln Gln Gly Ala Phe Trp Gly Lys Tyr Ala Gly
 100 105 110
 Val Phe Val Ser Thr Gly Thr Leu Gly Gly Gly Gln Glu Thr Thr Ala
 115 120 125
 Ile Thr Ser Met Ser Thr Leu Val Asp His Gly Phe Ile Tyr Val Pro
 130 135 140
 Leu Gly Tyr Lys Thr Ala Phe Ser Met Leu Ala Asn Leu Asp Glu Val
 145 150 155 160
 His Gly Gly Ser Pro Trp Gly Ala Gly Thr Phe Ser Ala Gly Asp Gly
 165 170 175
 Ser Arg Gln Pro Ser Glu Leu Glu Leu Asn Ile Ala Gln Ala Gln Gly
 180 185 190

-continued

Lys Ala Phe Tyr Glu Ala Val Ala Lys Ala His Gln
 195 200

<210> SEQ ID NO 11
 <211> LENGTH: 495
 <212> TYPE: PRT
 <213> ORGANISM: *Alternaria alternata*

<400> SEQUENCE: 11

Met Thr Ser Val Lys Leu Ser Thr Pro Gln Thr Gly Glu Phe Glu Gln
 1 5 10 15
 Pro Thr Gly Leu Phe Ile Asn Asn Glu Phe Val Lys Ala Val Asp Gly
 20 25 30
 Lys Thr Phe Asp Val Ile Asn Pro Ser Thr Glu Glu Val Ile Cys Ser
 35 40 45
 Val Gln Glu Ala Thr Glu Lys Asp Val Asp Ile Ala Val Ala Ala Ala
 50 55 60
 Arg Lys Ala Phe Asn Gly Pro Trp Ala Lys Glu Thr Pro Glu Asn Arg
 65 70 75 80
 Gly Lys Leu Leu Asn Lys Leu Ala Asp Leu Phe Glu Lys Asn Ala Asp
 85 90 95
 Leu Ile Ala Ala Val Glu Ala Leu Asp Asn Gly Lys Ala Phe Ser Met
 100 105 110
 Ala Lys Asn Val Asp Val Pro Ala Ala Ala Gly Cys Leu Arg Tyr Tyr
 115 120 125
 Gly Gly Trp Ala Asp Lys Ile Glu Gly Lys Val Val Asp Thr Ala Pro
 130 135 140
 Asp Ser Phe Asn Tyr Ile Arg Lys Ser Leu Leu Val Phe Ala Val Arg
 145 150 155 160
 Ser Ser Met Glu Leu Pro Ile Leu Met Trp Ser Trp Lys Ile Gly Pro
 165 170 175
 Ala Ile Ala Thr Gly Asn Thr Val Val Leu Lys Thr Ala Glu Gln Thr
 180 185 190
 Pro Leu Ser Ala Tyr Ile Ala Cys Lys Leu Ile Gln Glu Ala Gly Phe
 195 200 205
 Pro Pro Gly Val Ile Asn Val Ile Thr Gly Phe Gly Lys Ile Ala Gly
 210 215 220
 Ala Ala Met Ser Ala His Met Asp Ile Asp Lys Ile Ala Phe Thr Gly
 225 230 235 240
 Ser Thr Val Val Gly Arg Gln Ile Met Lys Ser Ala Ala Gly Ser Asn
 245 250 255
 Leu Lys Lys Val Thr Leu Glu Leu Gly Gly Lys Ser Pro Asn Ile Val
 260 265 270
 Phe Ala Asp Ala Asp Leu Asp Glu Ala Ile His Trp Val Asn Phe Gly
 275 280 285
 Ile Tyr Phe Asn His Gly Gln Ala Cys Cys Ala Gly Ser Arg Ile Tyr
 290 295 300
 Val Gln Glu Glu Ile Tyr Asp Lys Phe Ile Gln Arg Phe Lys Glu Arg
 305 310 315 320
 Ala Ala Gln Asn Ala Val Gly Asp Pro Phe Ala Ala Thr Leu Gln Gly
 325 330 335
 Pro Gln Val Ser Gln Leu Gln Phe Asp Arg Ile Met Gly Tyr Ile Glu
 340 345 350
 Glu Gly Lys Lys Ser Gly Ala Thr Ile Glu Thr Gly Gly Asn Arg Lys
 355 360 365

-continued

Gly Asp Lys Gly Tyr Phe Ile Glu Pro Thr Ile Phe Ser Asn Val Thr
 370 375 380
 Glu Asp Met Lys Ile Gln Gln Glu Glu Ile Phe Gly Pro Val Cys Thr
 385 390 395 400
 Ile Ser Lys Phe Lys Thr Lys Ala Asp Val Ile Lys Ile Gly Asn Asn
 405 410 415
 Thr Thr Tyr Gly Leu Ser Ala Ala Val His Thr Ser Asn Leu Thr Thr
 420 425 430
 Ala Ile Glu Val Ala Asn Ala Leu Arg Ala Gly Thr Val Trp Val Asn
 435 440 445
 Ser Tyr Asn Thr Leu His Trp Gln Leu Pro Phe Gly Gly Tyr Lys Glu
 450 455 460
 Ser Gly Ile Gly Arg Glu Leu Gly Glu Ala Ala Leu Asp Asn Tyr Ile
 465 470 475 480
 Gln Thr Lys Thr Val Ser Ile Arg Leu Gly Asp Val Leu Phe Gly
 485 490 495

<210> SEQ ID NO 12
 <211> LENGTH: 110
 <212> TYPE: PRT
 <213> ORGANISM: *Alternaria alternata*

<400> SEQUENCE: 12

Met Ser Thr Ser Glu Leu Ala Thr Ser Tyr Ala Ala Leu Ile Leu Ala
 1 5 10 15
 Asp Asp Gly Val Asp Ile Thr Ala Asp Lys Leu Gln Ser Leu Ile Lys
 20 25 30
 Ala Ala Lys Ile Glu Glu Val Glu Pro Ile Trp Thr Thr Leu Phe Ala
 35 40 45
 Lys Ala Leu Glu Gly Lys Asp Val Lys Asp Leu Leu Leu Asn Val Gly
 50 55 60
 Ser Gly Gly Gly Ala Ala Pro Leu Pro Glu Ala Leu Leu Leu Arg Trp
 65 70 75 80
 Arg Ala Ala Asp Ala Ala Pro Ala Ala Glu Glu Lys Lys Glu Glu Glu
 85 90 95
 Lys Glu Glu Ser Asp Glu Asp Met Gly Phe Gly Leu Phe Asp
 100 105 110

<210> SEQ ID NO 13
 <211> LENGTH: 396
 <212> TYPE: PRT
 <213> ORGANISM: *Ambrosia artemisiifolia* (Short ragweed)

<400> SEQUENCE: 13

Met Gly Ile Lys His Cys Cys Tyr Ile Leu Tyr Phe Thr Leu Ala Leu
 1 5 10 15
 Val Thr Leu Leu Gln Pro Val Arg Ser Ala Glu Asp Leu Gln Glu Ile
 20 25 30
 Leu Pro Val Asn Glu Thr Arg Arg Leu Thr Thr Ser Gly Ala Tyr Asn
 35 40 45
 Ile Ile Asp Gly Cys Trp Arg Gly Lys Ala Asp Trp Ala Glu Asn Arg
 50 55 60
 Lys Ala Leu Ala Asp Cys Ala Gln Gly Phe Gly Lys Gly Thr Val Gly
 65 70 75 80
 Gly Lys Asp Gly Asp Ile Tyr Thr Val Thr Ser Glu Leu Asp Asp Asp
 85 90 95

-continued

Val Ala Asn Pro Lys Glu Gly Thr Leu Arg Phe Gly Ala Ala Gln Asn
 100 105 110
 Arg Pro Leu Trp Ile Ile Phe Glu Arg Asp Met Val Ile Arg Leu Asp
 115 120 125
 Lys Glu Met Val Val Asn Ser Asp Lys Thr Ile Asp Gly Arg Gly Ala
 130 135 140
 Lys Val Glu Ile Ile Asn Ala Gly Phe Thr Leu Asn Gly Val Lys Asn
 145 150 155 160
 Val Ile Ile His Asn Ile Asn Met His Asp Val Lys Val Asn Pro Gly
 165 170 175
 Gly Leu Ile Lys Ser Asn Asp Gly Pro Ala Ala Pro Arg Ala Gly Ser
 180 185 190
 Asp Gly Asp Ala Ile Ser Ile Ser Gly Ser Ser Gln Ile Trp Ile Asp
 195 200 205
 His Cys Ser Leu Ser Lys Ser Val Asp Gly Leu Val Asp Ala Lys Leu
 210 215 220
 Gly Thr Thr Arg Leu Thr Val Ser Asn Ser Leu Phe Thr Gln His Gln
 225 230 235 240
 Phe Val Leu Leu Phe Gly Ala Gly Asp Glu Asn Ile Glu Asp Arg Gly
 245 250 255
 Met Leu Ala Thr Val Ala Phe Asn Thr Phe Thr Asp Asn Val Asp Gln
 260 265 270
 Arg Met Pro Arg Cys Arg His Gly Phe Phe Gln Val Val Asn Asn Asn
 275 280 285
 Tyr Asp Lys Trp Gly Ser Tyr Ala Ile Gly Gly Ser Ala Ser Pro Thr
 290 295 300
 Ile Leu Ser Gln Gly Asn Arg Phe Cys Ala Pro Asp Glu Arg Ser Lys
 305 310 315 320
 Lys Asn Val Leu Gly Arg His Gly Glu Ala Ala Ala Glu Ser Met Lys
 325 330 335
 Trp Asn Trp Arg Thr Asn Lys Asp Val Leu Glu Asn Gly Ala Ile Phe
 340 345 350
 Val Ala Ser Gly Val Asp Pro Val Leu Thr Pro Glu Gln Ser Ala Gly
 355 360 365
 Met Ile Pro Ala Glu Pro Gly Glu Ser Ala Leu Ser Leu Thr Ser Ser
 370 375 380
 Ala Gly Val Leu Ser Cys Gln Pro Gly Ala Pro Cys
 385 390 395

<210> SEQ ID NO 14

<211> LENGTH: 398

<212> TYPE: PRT

<213> ORGANISM: *Ambrosia artemisiifolia* (Short ragweed)

<400> SEQUENCE: 14

Met Gly Ile Lys His Cys Cys Tyr Ile Leu Tyr Phe Thr Leu Ala Leu
 1 5 10 15
 Val Thr Leu Leu Gln Pro Val Arg Ser Ala Glu Asp Val Glu Glu Phe
 20 25 30
 Leu Pro Ser Ala Asn Glu Thr Arg Arg Ser Leu Lys Ala Cys Glu Ala
 35 40 45
 His Asn Ile Ile Asp Lys Cys Trp Arg Cys Lys Ala Asp Trp Ala Asn
 50 55 60
 Asn Arg Gln Ala Leu Ala Asp Cys Ala Gln Gly Phe Ala Lys Gly Thr

-continued

65	70	75	80
Tyr Gly Gly Lys His Gly Asp Val Tyr Thr Val Thr Ser Asp Lys Asp	85	90	95
Asp Asp Val Ala Asn Pro Lys Glu Gly Thr Leu Arg Phe Ala Ala Ala	100	105	110
Gln Asn Arg Pro Leu Trp Ile Ile Phe Lys Arg Asn Met Val Ile His	115	120	125
Leu Asn Gln Glu Leu Val Val Asn Ser Asp Lys Thr Ile Asp Gly Arg	130	135	140
Gly Val Lys Val Asn Ile Val Asn Ala Gly Leu Thr Leu Met Asn Val	145	150	155
Lys Asn Ile Ile Ile His Asn Ile Asn Ile His Asp Ile Lys Val Cys	165	170	175
Pro Gly Gly Met Ile Lys Ser Asn Asp Gly Pro Pro Ile Leu Arg Gln	180	185	190
Gln Ser Asp Gly Asp Ala Ile Asn Val Ala Gly Ser Ser Gln Ile Trp	195	200	205
Ile Asp His Cys Ser Leu Ser Lys Ala Ser Asp Gly Leu Leu Asp Ile	210	215	220
Thr Leu Gly Ser Ser His Val Thr Val Ser Asn Cys Lys Phe Thr Gln	225	230	235
His Gln Phe Val Leu Leu Leu Gly Ala Asp Asp Thr His Tyr Gln Asp	245	250	255
Lys Gly Met Leu Ala Thr Val Ala Phe Asn Met Phe Thr Asp His Val	260	265	270
Asp Gln Arg Met Pro Arg Cys Arg Phe Gly Phe Phe Gln Val Val Asn	275	280	285
Asn Asn Tyr Asp Arg Trp Gly Thr Tyr Ala Ile Gly Gly Ser Ser Ala	290	295	300
Pro Thr Ile Leu Ser Gln Gly Asn Arg Phe Phe Ala Pro Asp Asp Ile	305	310	315
Ile Lys Lys Asn Val Leu Ala Arg Thr Gly Thr Gly Asn Ala Glu Ser	325	330	335
Met Ser Trp Asn Trp Arg Thr Asp Arg Asp Leu Leu Glu Asn Gly Ala	340	345	350
Ile Phe Leu Pro Ser Gly Ser Asp Pro Val Leu Thr Pro Glu Gln Lys	355	360	365
Ala Gly Met Ile Pro Ala Glu Pro Gly Glu Ala Val Leu Arg Leu Thr	370	375	380
Ser Ser Ala Gly Val Leu Ser Cys His Gln Gly Ala Pro Cys	385	390	395

<210> SEQ ID NO 15

<211> LENGTH: 397

<212> TYPE: PRT

<213> ORGANISM: Ambrosia artemisiifolia (Short ragweed)

<400> SEQUENCE: 15

Met Gly Ile Lys Gln Cys Cys Tyr Ile Leu Tyr Phe Thr Leu Ala Leu	1	5	10	15
Val Ala Leu Leu Gln Pro Val Arg Ser Ala Glu Gly Val Gly Glu Ile	20	25	30	
Leu Pro Ser Val Asn Glu Thr Arg Ser Leu Gln Ala Cys Glu Ala Leu	35	40	45	

-continued

Asn Ile Ile Asp Lys Cys Trp Arg Gly Lys Ala Asp Trp Glu Asn Asn
 50 55 60
 Arg Gln Ala Leu Ala Asp Cys Ala Gln Gly Phe Ala Lys Gly Thr Tyr
 65 70 75 80
 Gly Gly Lys Trp Gly Asp Val Tyr Thr Val Thr Ser Asn Leu Asp Asp
 85 90 95
 Asp Val Ala Asn Pro Lys Glu Gly Thr Leu Arg Phe Ala Ala Ala Gln
 100 105 110
 Asn Arg Pro Leu Trp Ile Ile Phe Lys Asn Asp Met Val Ile Asn Leu
 115 120 125
 Asn Gln Glu Leu Val Val Asn Ser Asp Lys Thr Ile Asp Gly Arg Gly
 130 135 140
 Val Lys Val Glu Ile Ile Asn Gly Gly Leu Thr Leu Met Asn Val Lys
 145 150 155 160
 Asn Ile Ile Ile His Asn Ile Asn Ile His Asp Val Lys Val Leu Pro
 165 170 175
 Gly Gly Met Ile Lys Ser Asn Asp Gly Pro Pro Ile Leu Arg Gln Ala
 180 185 190
 Ser Asp Gly Asp Thr Ile Asn Val Ala Gly Ser Ser Gln Ile Trp Ile
 195 200 205
 Asp His Cys Ser Leu Ser Lys Ser Phe Asp Gly Leu Val Asp Val Thr
 210 215 220
 Leu Gly Ser Thr His Val Thr Ile Ser Asn Cys Lys Phe Thr Gln Gln
 225 230 235 240
 Ser Lys Ala Ile Leu Leu Gly Ala Asp Asp Thr His Val Gln Asp Lys
 245 250 255
 Gly Met Leu Ala Thr Val Ala Phe Asn Met Phe Thr Asp Asn Val Asp
 260 265 270
 Gln Arg Met Pro Arg Cys Arg Phe Gly Phe Phe Gln Val Val Asn Asn
 275 280 285
 Asn Tyr Asp Arg Trp Gly Thr Tyr Ala Ile Gly Gly Ser Ser Ala Pro
 290 295 300
 Thr Ile Leu Cys Gln Gly Asn Arg Phe Leu Ala Pro Asp Asp Gln Ile
 305 310 315 320
 Lys Lys Asn Val Leu Ala Arg Thr Gly Thr Gly Ala Ala Glu Ser Met
 325 330 335
 Ala Trp Asn Trp Arg Ser Asp Lys Asp Leu Leu Glu Asn Gly Ala Ile
 340 345 350
 Phe Val Thr Ser Gly Ser Asp Pro Val Leu Thr Pro Val Gln Ser Ala
 355 360 365
 Gly Met Ile Pro Ala Glu Pro Gly Glu Ala Ala Ile Lys Leu Thr Ser
 370 375 380
 Ser Ala Gly Val Phe Ser Cys His Pro Gly Ala Pro Cys
 385 390 395

<210> SEQ ID NO 16

<211> LENGTH: 392

<212> TYPE: PRT

<213> ORGANISM: Ambrosia artemisiifolia (Short ragweed)

<400> SEQUENCE: 16

Met Gly Ile Lys His Cys Cys Tyr Ile Leu Tyr Phe Thr Leu Ala Leu
 1 5 10 15
 Val Thr Leu Leu Gln Pro Val Arg Ser Ala Glu Asp Leu Gln Gln Ile
 20 25 30

-continued

Leu Pro Ser Ala Asn Glu Thr Arg Ser Leu Thr Thr Cys Gly Thr Tyr
 35 40 45
 Asn Ile Ile Asp Gly Cys Trp Arg Gly Lys Ala Asp Trp Ala Glu Asn
 50 55 60
 Arg Lys Ala Leu Ala Asp Cys Ala Gln Gly Phe Ala Lys Gly Thr Ile
 65 70 75 80
 Gly Gly Lys Asp Gly Asp Ile Tyr Thr Val Thr Ser Glu Leu Asp Asp
 85 90 95
 Asp Val Ala Asn Pro Lys Glu Gly Thr Leu Arg Phe Gly Ala Ala Gln
 100 105 110
 Asn Arg Pro Leu Trp Ile Ile Phe Ala Arg Asp Met Val Ile Arg Leu
 115 120 125
 Asp Arg Glu Leu Ala Ile Asn Asn Asp Lys Thr Ile Asp Gly Arg Gly
 130 135 140
 Ala Lys Val Glu Ile Ile Asn Ala Gly Phe Ala Ile Tyr Asn Val Lys
 145 150 155 160
 Asn Ile Ile Ile His Asn Ile Ile Met His Asp Ile Val Val Asn Pro
 165 170 175
 Gly Gly Leu Ile Lys Ser His Asp Gly Pro Pro Val Pro Arg Lys Gly
 180 185 190
 Ser Asp Gly Asp Ala Ile Gly Ile Ser Gly Gly Ser Gln Ile Trp Ile
 195 200 205
 Asp His Cys Ser Leu Ser Lys Ala Val Asp Gly Leu Ile Asp Ala Lys
 210 215 220
 His Gly Ser Thr His Phe Thr Val Ser Asn Cys Leu Phe Thr Gln His
 225 230 235 240
 Gln Tyr Leu Leu Leu Phe Trp Asp Phe Asp Glu Arg Gly Met Leu Cys
 245 250 255
 Thr Val Ala Phe Asn Lys Phe Thr Asp Asn Val Asp Gln Arg Met Pro
 260 265 270
 Asn Leu Arg His Gly Phe Val Gln Val Val Asn Asn Asn Tyr Glu Arg
 275 280 285
 Trp Gly Ser Tyr Ala Leu Gly Gly Ser Ala Gly Pro Thr Ile Leu Ser
 290 295 300
 Gln Gly Asn Arg Phe Leu Ala Ser Asp Ile Lys Lys Glu Val Val Gly
 305 310 315 320
 Arg Tyr Gly Glu Ser Ala Met Ser Glu Ser Ile Asn Trp Asn Trp Arg
 325 330 335
 Ser Tyr Met Asp Val Phe Glu Asn Gly Ala Ile Phe Val Pro Ser Gly
 340 345 350
 Val Asp Pro Val Leu Thr Pro Glu Gln Asn Ala Gly Met Ile Pro Ala
 355 360 365
 Glu Pro Gly Glu Ala Val Leu Arg Leu Thr Ser Ser Ala Gly Val Leu
 370 375 380
 Ser Cys Gln Pro Gly Ala Pro Cys
 385 390

<210> SEQ ID NO 17

<211> LENGTH: 397

<212> TYPE: PRT

<213> ORGANISM: Ambrosia artemisiifolia (Short ragweed)

<400> SEQUENCE: 17

Met Gly Ile Lys His Cys Cys Tyr Ile Leu Tyr Phe Thr Leu Ala Leu

-continued

1	5	10	15
Val Thr Leu Val Gln Ala Gly Arg Leu Gly Glu Glu Val Asp Ile Leu	20	25	30
Pro Ser Pro Asn Asp Thr Arg Arg Ser Leu Gln Gly Cys Glu Ala His	35	40	45
Asn Ile Ile Asp Lys Cys Trp Arg Cys Lys Pro Asp Trp Ala Glu Asn	50	55	60
Arg Gln Ala Leu Gly Asn Cys Ala Gln Gly Phe Gly Lys Ala Thr His	65	70	80
Gly Gly Lys Trp Gly Asp Ile Tyr Met Val Thr Ser Asp Gln Asp Asp	85	90	95
Asp Val Val Asn Pro Lys Glu Gly Thr Leu Arg Phe Gly Ala Thr Gln	100	105	110
Asp Arg Pro Leu Trp Ile Ile Phe Gln Arg Asp Met Ile Ile Tyr Leu	115	120	125
Gln Gln Glu Met Val Val Thr Ser Asp Lys Thr Ile Asp Gly Arg Gly	130	135	140
Ala Lys Val Glu Leu Val Tyr Gly Gly Ile Thr Leu Met Asn Val Lys	145	150	160
Asn Val Ile Ile His Asn Ile Asp Ile His Asp Val Arg Val Leu Pro	165	170	175
Gly Gly Arg Ile Lys Ser Asn Gly Gly Pro Ala Ile Pro Arg His Gln	180	185	190
Ser Asp Gly Asp Ala Ile His Val Thr Gly Ser Ser Asp Ile Trp Ile	195	200	205
Asp His Cys Thr Leu Ser Lys Ser Phe Asp Gly Leu Val Asp Val Asn	210	215	220
Trp Gly Ser Thr Gly Val Thr Ile Ser Asn Cys Lys Phe Thr His His	225	230	240
Glu Lys Ala Val Leu Leu Gly Ala Ser Asp Thr His Phe Gln Asp Leu	245	250	255
Lys Met His Val Thr Leu Ala Tyr Asn Ile Phe Thr Asn Thr Val His	260	265	270
Glu Arg Met Pro Arg Cys Arg Phe Gly Phe Phe Gln Ile Val Asn Asn	275	280	285
Phe Tyr Asp Arg Trp Asp Lys Tyr Ala Ile Gly Gly Ser Ser Asn Pro	290	295	300
Thr Ile Leu Ser Gln Gly Asn Lys Phe Val Ala Pro Asp Phe Ile Tyr	305	310	320
Lys Lys Asn Val Cys Leu Arg Thr Gly Ala Gln Glu Pro Glu Trp Met	325	330	335
Thr Trp Asn Trp Arg Thr Gln Asn Asp Val Leu Glu Asn Gly Ala Ile	340	345	350
Phe Val Ala Ser Gly Ser Asp Pro Val Leu Thr Ala Glu Gln Asn Ala	355	360	365
Gly Met Met Gln Ala Glu Pro Gly Asp Met Val Pro Gln Leu Thr Met	370	375	380
Asn Ala Gly Val Leu Thr Cys Ser Pro Gly Ala Pro Cys	385	390	395

<210> SEQ ID NO 18

<211> LENGTH: 101

<212> TYPE: PRT

<213> ORGANISM: Ambrosia artemisiifolia var. elatior (Short ragweed)

-continued

<400> SEQUENCE: 18

Gly Lys Val Tyr Leu Val Gly Gly Pro Glu Leu Gly Gly Trp Lys Leu
 1 5 10 15
 Gln Ser Asp Pro Arg Ala Tyr Ala Leu Trp Ser Ala Arg Gln Gln Phe
 20 25 30
 Lys Thr Thr Asp Val Leu Trp Phe Asn Phe Thr Thr Gly Glu Asp Ser
 35 40 45
 Val Ala Glu Val Trp Arg Glu Glu Ala Tyr His Ala Cys Asp Ile Lys
 50 55 60
 Asp Pro Ile Arg Leu Glu Pro Gly Gly Pro Asp Arg Phe Thr Leu Leu
 65 70 75 80
 Thr Pro Gly Ser His Phe Ile Cys Thr Lys Asp Gln Lys Phe Val Ala
 85 90 95
 Cys Val Pro Gly Arg
 100

<210> SEQ ID NO 19

<211> LENGTH: 45

<212> TYPE: PRT

<213> ORGANISM: *Ambrosia artemisiifolia* var. *elatior* (Short ragweed)

<400> SEQUENCE: 19

Leu Val Pro Cys Ala Trp Ala Gly Asn Val Cys Gly Glu Lys Arg Ala
 1 5 10 15
 Tyr Cys Cys Ser Asp Pro Gly Arg Tyr Cys Pro Trp Gln Val Val Cys
 20 25 30
 Tyr Glu Ser Ser Glu Ile Cys Ser Lys Lys Cys Gly Lys
 35 40 45

<210> SEQ ID NO 20

<211> LENGTH: 77

<212> TYPE: PRT

<213> ORGANISM: *Ambrosia psilostachya* (Western ragweed)

<400> SEQUENCE: 20

Met Asn Asn Glu Lys Asn Val Ser Phe Glu Phe Ile Gly Ser Thr Asp
 1 5 10 15
 Glu Val Asp Glu Ile Lys Leu Leu Pro Cys Ala Trp Ala Gly Asn Val
 20 25 30
 Cys Gly Glu Lys Arg Ala Tyr Cys Cys Ser Asp Pro Gly Arg Tyr Cys
 35 40 45
 Pro Trp Gln Val Val Cys Tyr Glu Ser Ser Glu Ile Cys Ser Gln Lys
 50 55 60
 Cys Gly Lys Met Arg Met Asn Val Thr Lys Asn Thr Ile
 65 70 75

<210> SEQ ID NO 21

<211> LENGTH: 77

<212> TYPE: PRT

<213> ORGANISM: *Ambrosia psilostachya* (Western ragweed)

<400> SEQUENCE: 21

Met Asn Asn Glu Lys Asn Val Ser Phe Glu Phe Ile Gly Ser Thr Asn
 1 5 10 15
 Glu Val Asp Glu Ile Lys Val Met Ala Cys Tyr Ala Ala Gly Ser Ile
 20 25 30
 Cys Gly Glu Lys Arg Gly Tyr Cys Ser Ser Asp Pro Gly Arg Tyr Cys

-continued

```

      35          40          45
Pro Trp Gln Val Val Cys Tyr Glu Ser Arg Lys Ile Cys Ala Lys Asn
  50          55          60

Ala Ala Lys Met Arg Met Asn Val Thr Lys Asn Thr Ile
  65          70          75

```

```

<210> SEQ ID NO 22
<211> LENGTH: 73
<212> TYPE: PRT
<213> ORGANISM: Ambrosia trifida (Giant ragweed)

```

```

<400> SEQUENCE: 22

```

```

Met Lys Asn Ile Phe Met Leu Thr Leu Phe Ile Leu Ile Ile Thr Ser
  1          5          10          15

Thr Ile Lys Ala Ile Gly Ser Thr Asn Glu Val Asp Glu Ile Lys Gln
          20          25          30

Glu Asp Asp Gly Leu Cys Tyr Glu Gly Thr Asn Cys Gly Lys Val Gly
          35          40          45

Lys Tyr Cys Cys Ser Pro Ile Gly Lys Tyr Cys Val Cys Tyr Asp Ser
          50          55          60

Lys Ala Ile Cys Asn Lys Asn Cys Thr
  65          70

```

```

<210> SEQ ID NO 23
<211> LENGTH: 154
<212> TYPE: PRT
<213> ORGANISM: um graveolens (Celery)

```

```

<400> SEQUENCE: 23

```

```

Met Gly Val Gln Thr His Val Leu Glu Leu Thr Ser Ser Val Ser Ala
  1          5          10          15

Glu Lys Ile Phe Gln Gly Phe Val Ile Asp Val Asp Thr Val Leu Pro
          20          25          30

Lys Ala Ala Pro Gly Ala Tyr Lys Ser Val Glu Ile Lys Gly Asp Gly
          35          40          45

Gly Pro Gly Thr Leu Lys Ile Ile Thr Leu Pro Asp Gly Gly Pro Ile
          50          55          60

Thr Thr Met Thr Leu Arg Ile Asp Gly Val Asn Lys Glu Ala Leu Thr
  65          70          75          80

Phe Asp Tyr Ser Val Ile Asp Gly Asp Ile Leu Leu Gly Phe Ile Glu
          85          90          95

Ser Ile Glu Asn His Val Val Leu Val Pro Thr Ala Asp Gly Gly Ser
          100          105          110

Ile Cys Lys Thr Thr Ala Ile Phe His Thr Lys Gly Asp Ala Val Val
          115          120          125

Pro Glu Glu Asn Ile Lys Tyr Ala Asn Glu Gln Asn Thr Ala Leu Phe
          130          135          140

Lys Ala Leu Glu Ala Tyr Leu Ile Ala Asn
          145          150

```

```

<210> SEQ ID NO 24
<211> LENGTH: 162
<212> TYPE: PRT
<213> ORGANISM: Apis mellifera (Honeybee)

```

```

<400> SEQUENCE: 24

```

```

Gly Ser Leu Phe Leu Leu Leu Ser Thr Ser His Gly Trp Gln Ile
  1          5          10          15

```

-continued

Arg Asp Arg Ile Gly Asp Asn Glu Leu Glu Glu Arg Ile Ile Tyr Pro
 20 25 30
 Gly Thr Leu Trp Cys Gly His Gly Asn Lys Ser Ser Gly Pro Asn Glu
 35 40 45
 Leu Gly Arg Phe Lys His Thr Asp Ala Cys Cys Arg Thr His Asp Met
 50 55 60
 Cys Pro Asp Val Met Ser Ala Gly Glu Ser Lys His Gly Leu Thr Asn
 65 70 75 80
 Thr Ala Ser His Thr Arg Leu Ser Cys Asp Cys Asp Asp Lys Phe Tyr
 85 90 95
 Asp Cys Leu Lys Asn Ser Ala Asp Thr Ile Ser Ser Tyr Phe Val Gly
 100 105 110
 Lys Met Tyr Phe Asn Leu Ile Asp Thr Lys Cys Tyr Lys Leu Glu His
 115 120 125
 Pro Val Thr Gly Cys Gly Glu Arg Thr Glu Gly Arg Cys Leu His Tyr
 130 135 140
 Thr Val Asp Lys Ser Lys Pro Lys Val Tyr Gln Trp Phe Asp Leu Arg
 145 150 155 160
 Lys Tyr

<210> SEQ ID NO 25
 <211> LENGTH: 382
 <212> TYPE: PRT
 <213> ORGANISM: Apis mellifera (Honeybee)

<400> SEQUENCE: 25

Met Ser Arg Pro Leu Val Ile Thr Glu Gly Met Met Ile Gly Val Leu
 1 5 10 15
 Leu Met Leu Ala Pro Ile Asn Ala Leu Leu Leu Gly Phe Val Gln Ser
 20 25 30
 Thr Pro Asp Asn Asn Lys Thr Val Arg Glu Phe Asn Val Tyr Trp Asn
 35 40 45
 Val Pro Thr Phe Met Cys His Lys Tyr Gly Leu Arg Phe Glu Glu Val
 50 55 60
 Ser Glu Lys Tyr Gly Ile Leu Gln Asn Trp Met Asp Lys Phe Arg Gly
 65 70 75 80
 Glu Glu Ile Ala Ile Leu Tyr Asp Pro Gly Met Phe Pro Ala Leu Leu
 85 90 95
 Lys Asp Pro Asn Gly Asn Val Val Ala Arg Asn Gly Gly Val Pro Gln
 100 105 110
 Leu Gly Asn Leu Thr Lys His Leu Gln Val Phe Arg Asp His Leu Ile
 115 120 125
 Asn Gln Ile Pro Asp Lys Ser Phe Pro Gly Val Gly Val Ile Asp Phe
 130 135 140
 Glu Ser Trp Arg Pro Ile Phe Arg Gln Asn Trp Ala Ser Leu Gln Pro
 145 150 155 160
 Tyr Lys Lys Leu Ser Val Glu Val Val Arg Arg Glu His Pro Phe Trp
 165 170 175
 Asp Asp Gln Arg Val Glu Gln Glu Ala Lys Arg Arg Phe Glu Lys Tyr
 180 185 190
 Gly Gln Leu Phe Met Glu Glu Thr Leu Lys Ala Ala Lys Arg Met Arg
 195 200 205
 Pro Ala Ala Asn Trp Gly Tyr Tyr Ala Tyr Pro Tyr Cys Tyr Asn Leu
 210 215 220

-continued

Thr Pro Asn Gln Pro Ser Ala Gln Cys Glu Ala Thr Thr Met Gln Glu
 225 230 235 240
 Asn Asp Lys Met Ser Trp Leu Phe Glu Ser Glu Asp Val Leu Leu Pro
 245 250 255
 Ser Val Tyr Leu Arg Trp Asn Leu Thr Ser Gly Glu Arg Val Gly Leu
 260 265 270
 Val Gly Gly Arg Val Lys Glu Ala Leu Arg Ile Ala Arg Gln Met Thr
 275 280 285
 Thr Ser Arg Lys Lys Val Leu Pro Tyr Tyr Trp Tyr Lys Tyr Gln Asp
 290 295 300
 Arg Arg Asp Thr Asp Leu Ser Arg Ala Asp Leu Glu Ala Thr Leu Arg
 305 310 315 320
 Lys Ile Thr Asp Leu Gly Ala Asp Gly Phe Ile Ile Trp Gly Ser Ser
 325 330 335
 Asp Asp Ile Asn Thr Lys Ala Lys Cys Leu Gln Phe Arg Glu Tyr Leu
 340 345 350
 Asn Asn Glu Leu Gly Pro Ala Val Lys Arg Ile Ala Leu Asn Asn Asn
 355 360 365
 Ala Asn Asp Arg Leu Thr Val Asp Val Ser Val Asp Gln Val
 370 375 380

<210> SEQ ID NO 26
 <211> LENGTH: 70
 <212> TYPE: PRT
 <213> ORGANISM: Apis mellifera (Honeybee) Apis cerana (Ind. honeybee)
 <400> SEQUENCE: 26

Met Lys Phe Leu Val Asn Val Ala Leu Val Phe Met Val Val Tyr Ile
 1 5 10 15
 Ser Tyr Ile Tyr Ala Ala Pro Glu Pro Glu Pro Ala Pro Glu Pro Glu
 20 25 30
 Ala Glu Ala Asp Ala Glu Ala Asp Pro Glu Ala Gly Ile Gly Ala Val
 35 40 45
 Leu Lys Val Leu Thr Thr Gly Leu Pro Ala Leu Ile Ser Trp Ile Lys
 50 55 60
 Arg Lys Arg Gln Gln Gly
 65 70

<210> SEQ ID NO 27
 <211> LENGTH: 614
 <212> TYPE: PRT
 <213> ORGANISM: Arachis hypogaea (Peanut)
 <400> SEQUENCE: 27

Met Arg Gly Arg Val Ser Pro Leu Met Leu Leu Leu Gly Ile Leu Val
 1 5 10 15
 Leu Ala Ser Val Ser Ala Thr Gln Ala Lys Ser Pro Tyr Arg Lys Thr
 20 25 30
 Glu Asn Pro Cys Ala Gln Arg Cys Leu Gln Ser Cys Gln Gln Glu Pro
 35 40 45
 Asp Asp Leu Lys Gln Lys Ala Cys Glu Ser Arg Cys Thr Lys Leu Glu
 50 55 60
 Tyr Asp Pro Arg Cys Val Tyr Asp Thr Gly Ala Thr Asn Gln Arg His
 65 70 75 80
 Pro Pro Gly Glu Arg Thr Arg Gly Arg Gln Pro Gly Asp Tyr Asp Asp
 85 90 95

-continued

Asp Arg Arg Gln Pro Arg Arg Glu Glu Gly Gly Arg Trp Gly Pro Ala
 100 105 110
 Glu Pro Arg Glu Arg Glu Arg Glu Glu Asp Trp Arg Gln Pro Arg Glu
 115 120 125
 Asp Trp Arg Arg Pro Ser His Gln Gln Pro Arg Lys Ile Arg Pro Glu
 130 135 140
 Gly Arg Glu Gly Glu Gln Glu Trp Gly Thr Pro Gly Ser Glu Val Arg
 145 150 155 160
 Glu Glu Thr Ser Arg Asn Asn Pro Phe Tyr Phe Pro Ser Arg Arg Phe
 165 170 175
 Ser Thr Arg Tyr Gly Asn Gln Asn Gly Arg Ile Arg Val Leu Gln Arg
 180 185 190
 Phe Asp Gln Arg Ser Lys Gln Phe Gln Asn Leu Gln Asn His Arg Ile
 195 200 205
 Val Gln Ile Glu Ala Arg Pro Asn Thr Leu Val Leu Pro Lys His Ala
 210 215 220
 Asp Ala Asp Asn Ile Leu Val Ile Gln Gln Gly Gln Ala Thr Val Thr
 225 230 235 240
 Val Ala Asn Gly Asn Asn Arg Lys Ser Phe Asn Leu Asp Glu Gly His
 245 250 255
 Ala Leu Arg Ile Pro Ser Gly Phe Ile Ser Tyr Ile Leu Asn Arg His
 260 265 270
 Asp Asn Gln Asn Leu Arg Val Ala Lys Ile Ser Met Pro Val Asn Thr
 275 280 285
 Pro Gly Gln Phe Glu Asp Phe Phe Pro Ala Ser Ser Arg Asp Gln Ser
 290 295 300
 Ser Tyr Leu Gln Gly Phe Ser Arg Asn Thr Leu Glu Ala Ala Phe Asn
 305 310 315 320
 Ala Glu Phe Asn Glu Ile Arg Arg Val Leu Leu Glu Glu Asn Ala Gly
 325 330 335
 Gly Glu Gln Glu Glu Arg Gly Gln Arg Arg Arg Ser Thr Arg Ser Ser
 340 345 350
 Asp Asn Glu Gly Val Ile Val Lys Val Ser Lys Glu His Val Gln Glu
 355 360 365
 Leu Thr Lys His Ala Lys Ser Val Ser Lys Lys Gly Ser Glu Glu Glu
 370 375 380
 Asp Ile Thr Asn Pro Ile Asn Leu Arg Asp Gly Glu Pro Asp Leu Ser
 385 390 395 400
 Asn Asn Phe Gly Arg Leu Phe Glu Val Lys Pro Asp Lys Lys Asn Pro
 405 410 415
 Gln Leu Gln Asp Leu Asp Met Met Leu Thr Cys Val Glu Ile Lys Glu
 420 425 430
 Gly Ala Leu Met Leu Pro His Phe Asn Ser Lys Ala Met Val Ile Val
 435 440 445
 Val Val Asn Lys Gly Thr Gly Asn Leu Glu Leu Val Ala Val Arg Lys
 450 455 460
 Glu Gln Gln Gln Arg Gly Arg Arg Glu Gln Glu Trp Glu Glu Glu Glu
 465 470 475 480
 Glu Asp Glu Glu Glu Glu Gly Ser Asn Arg Glu Val Arg Arg Tyr Thr
 485 490 495
 Ala Arg Leu Lys Glu Gly Asp Val Phe Ile Met Pro Ala Ala His Pro
 500 505 510

-continued

Val Ala Ile Asn Ala Ser Ser Glu Leu His Leu Leu Gly Phe Gly Ile
515 520 525

Asn Ala Glu Asn Asn His Arg Ile Phe Leu Ala Gly Asp Lys Asp Asn
530 535 540

Val Ile Asp Gln Ile Glu Lys Gln Ala Lys Asp Leu Ala Phe Pro Gly
545 550 555 560

Ser Gly Glu Gln Val Glu Lys Leu Ile Lys Asn Gln Arg Glu Ser His
565 570 575

Phe Val Ser Ala Arg Pro Gln Ser Gln Ser Pro Ser Ser Pro Glu Lys
580 585 590

Glu Asp Gln Glu Glu Glu Asn Gln Gly Gly Lys Gly Pro Leu Leu Ser
595 600 605

Ile Leu Lys Ala Phe Asn
610

<210> SEQ ID NO 28

<211> LENGTH: 626

<212> TYPE: PRT

<213> ORGANISM: Arachis hypogaea (Peanut)

<400> SEQUENCE: 28

Met Arg Gly Arg Val Ser Pro Leu Met Leu Leu Leu Gly Ile Leu Val
1 5 10 15

Leu Ala Ser Val Ser Ala Thr His Ala Lys Ser Ser Pro Tyr Gln Lys
20 25 30

Lys Thr Glu Asn Pro Cys Ala Gln Arg Cys Leu Gln Ser Cys Gln Gln
35 40 45

Glu Pro Asp Asp Leu Lys Gln Lys Ala Cys Glu Ser Arg Cys Thr Lys
50 55 60

Leu Glu Tyr Asp Pro Arg Cys Val Tyr Asp Pro Arg Gly His Thr Gly
65 70 75 80

Thr Thr Asn Gln Arg Ser Pro Pro Gly Glu Arg Thr Arg Gly Arg Gln
85 90 95

Pro Gly Asp Tyr Asp Asp Asp Arg Arg Gln Pro Arg Arg Glu Glu Gly
100 105 110

Gly Arg Trp Gly Pro Ala Gly Pro Arg Glu Arg Glu Arg Glu Glu Asp
115 120 125

Trp Arg Gln Pro Arg Glu Asp Trp Arg Arg Pro Ser His Gln Gln Pro
130 135 140

Arg Lys Ile Arg Pro Glu Gly Arg Glu Gly Glu Gln Glu Trp Gly Thr
145 150 155 160

Pro Gly Ser His Val Arg Glu Glu Thr Ser Arg Asn Asn Pro Phe Tyr
165 170 175

Phe Pro Ser Arg Arg Phe Ser Thr Arg Tyr Gly Asn Gln Asn Gly Arg
180 185 190

Ile Arg Val Leu Gln Arg Phe Asp Gln Arg Ser Arg Gln Phe Gln Asn
195 200 205

Leu Gln Asn His Arg Ile Val Gln Ile Glu Ala Lys Pro Asn Thr Leu
210 215 220

Val Leu Pro Lys His Ala Asp Ala Asp Asn Ile Leu Val Ile Gln Gln
225 230 235 240

Gly Gln Ala Thr Val Thr Val Ala Asn Gly Asn Asn Arg Lys Ser Phe
245 250 255

Asn Leu Asp Glu Gly His Ala Leu Arg Ile Pro Ser Gly Phe Ile Ser
260 265 270

-continued

1	5	10	15
Gly Asn His Leu Thr Ala Ala Ala Ile Leu Gly Gln Asp Gly Ser Val	20	25	30
Trp Ala Gln Ser Ala Lys Phe Pro Gln Leu Lys Pro Gln Glu Ile Asp	35	40	45
Gly Ile Lys Lys Asp Phe Glu Glu Pro Gly Phe Leu Ala Pro Thr Gly	50	55	60
Leu Phe Leu Gly Gly Glu Lys Tyr Met Val Ile Gln Gly Glu Gln Gly	65	70	75
Ala Val Ile Arg Gly Lys Lys Gly Pro Gly Gly Val Thr Ile Lys Lys	85	90	95
Thr Asn Gln Ala Leu Val Phe Gly Phe Tyr Asp Glu Pro Met Thr Gly	100	105	110
Gly Gln Cys Asn Leu Val Val Glu Arg Leu Gly Asp Tyr Leu Ile Glu	115	120	125
Ser Glu Leu	130		

<210> SEQ ID NO 30
 <211> LENGTH: 176
 <212> TYPE: PRT
 <213> ORGANISM: Aspergillus restrictus Aspergillus fumigatus

<400> SEQUENCE: 30

Met Val Ala Ile Lys Asn Leu Phe Leu Leu Ala Ala Thr Ala Val Ser	1	5	10	15
Val Leu Ala Ala Pro Ser Pro Leu Asp Ala Arg Ala Thr Trp Thr Cys	20	25	30	
Ile Asn Gln Gln Leu Asn Pro Lys Thr Asn Lys Trp Glu Asp Lys Arg	35	40	45	
Leu Leu Tyr Ser Gln Ala Lys Ala Glu Ser Asn Ser His His Ala Pro	50	55	60	
Leu Ser Asp Gly Lys Thr Gly Ser Ser Tyr Pro His Trp Phe Thr Asn	65	70	75	80
Gly Tyr Asp Gly Asn Gly Lys Leu Ile Lys Gly Arg Thr Pro Ile Lys	85	90	95	
Phe Gly Lys Ala Asp Cys Asp Arg Pro Pro Lys His Ser Gln Asn Gly	100	105	110	
Met Gly Lys Asp Asp His Tyr Leu Leu Glu Phe Pro Thr Phe Pro Asp	115	120	125	
Gly His Asp Tyr Lys Phe Asp Ser Lys Lys Pro Lys Glu Asp Pro Gly	130	135	140	
Pro Ala Arg Val Ile Tyr Thr Tyr Pro Asn Lys Val Phe Cys Gly Ile	145	150	155	160
Val Ala His Gln Arg Gly Asn Gln Gly Asp Leu Arg Leu Cys Ser His	165	170	175	

<210> SEQ ID NO 31
 <211> LENGTH: 310
 <212> TYPE: PRT
 <213> ORGANISM: Aspergillus fumigatus (Sartorya fumigata)

<400> SEQUENCE: 31

Met Ala Ala Leu Leu Arg Leu Ala Val Leu Leu Pro Leu Ala Ala Pro	1	5	10	15
Leu Val Ala Thr Leu Pro Thr Ser Pro Val Pro Ile Ala Ala Arg Ala				

-continued

20				25				30							
Thr	Pro	His	Glu	Pro	Val	Phe	Phe	Ser	Trp	Asp	Ala	Gly	Ala	Val	Thr
		35					40					45			
Ser	Phe	Pro	Ile	His	Ser	Ser	Cys	Asn	Ala	Thr	Gln	Arg	Arg	Gln	Ile
	50					55					60				
Glu	Ala	Gly	Leu	Asn	Glu	Ala	Val	Glu	Leu	Ala	Arg	His	Ala	Lys	Ala
65					70					75					80
His	Ile	Leu	Arg	Trp	Gly	Asn	Glu	Ser	Glu	Ile	Tyr	Arg	Lys	Tyr	Phe
				85					90					95	
Gly	Asn	Arg	Pro	Thr	Met	Glu	Ala	Val	Gly	Ala	Tyr	Asp	Val	Ile	Val
			100						105				110		
Asn	Gly	Asp	Lys	Ala	Asn	Val	Leu	Phe	Arg	Cys	Asp	Asn	Pro	Asp	Gly
		115					120					125			
Asn	Cys	Ala	Leu	Glu	Gly	Trp	Gly	Gly	His	Trp	Arg	Gly	Ala	Asn	Ala
		130					135				140				
Thr	Ser	Glu	Thr	Val	Ile	Cys	Asp	Arg	Ser	Tyr	Thr	Thr	Arg	Arg	Trp
145					150					155					160
Leu	Val	Ser	Met	Cys	Ser	Gln	Gly	Tyr	Thr	Val	Ala	Gly	Ser	Glu	Thr
				165					170					175	
Asn	Thr	Phe	Trp	Ala	Ser	Asp	Leu	Met	His	Arg	Leu	Tyr	His	Val	Pro
			180						185				190		
Ala	Val	Gly	Gln	Gly	Trp	Val	Asp	His	Phe	Ala	Asp	Gly	Tyr	Asp	Glu
		195					200					205			
Val	Ile	Ala	Leu	Ala	Lys	Ser	Asn	Gly	Thr	Glu	Ser	Thr	His	Asp	Ser
		210				215					220				
Glu	Ala	Phe	Glu	Tyr	Phe	Ala	Leu	Glu	Ala	Tyr	Ala	Phe	Asp	Ile	Ala
225					230					235				240	
Ala	Pro	Gly	Val	Gly	Cys	Ala	Gly	Glu	Ser	His	Gly	Pro	Asp	Gln	Gly
				245					250					255	
His	Asp	Thr	Gly	Ser	Ala	Ser	Ala	Pro	Ala	Ser	Thr	Ser	Thr	Ser	Ser
			260						265				270		
Ser	Ser	Ser	Gly	Ser	Gly	Ser	Gly	Ala	Thr	Thr	Thr	Pro	Thr	Asp	Ser
		275					280						285		
Pro	Ser	Ala	Thr	Ile	Asp	Val	Pro	Ser	Asn	Cys	His	Thr	His	Glu	Gly
		290				295					300				
Gly	Gln	Leu	His	Cys	Thr										
305					310										

<210> SEQ ID NO 32

<211> LENGTH: 168

<212> TYPE: PRT

<213> ORGANISM: Aspergillus fumigatus (Sartorya fumigata)

<400> SEQUENCE: 32

Met	Ser	Gly	Leu	Lys	Ala	Gly	Asp	Ser	Phe	Pro	Ser	Asp	Val	Val	Phe
1				5					10					15	
Ser	Tyr	Ile	Pro	Trp	Ser	Glu	Asp	Lys	Gly	Glu	Ile	Thr	Ala	Cys	Gly
			20						25				30		
Ile	Pro	Ile	Asn	Tyr	Asn	Ala	Ser	Lys	Glu	Trp	Ala	Asp	Lys	Lys	Val
		35					40					45			
Ile	Leu	Phe	Ala	Leu	Pro	Gly	Ala	Phe	Thr	Pro	Val	Cys	Ser	Ala	Arg
		50				55					60				
His	Val	Pro	Glu	Tyr	Ile	Glu	Lys	Leu	Pro	Glu	Ile	Arg	Ala	Lys	Gly
65					70					75					80

-continued

Tyr Asn Tyr Ser Val Ile Glu Gly Gly Pro Ile Gly Asp Thr Leu Glu
85 90 95

Lys Ile Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly Gly Ser
100 105 110

Ile Leu Lys Ile Ser Asn Lys Tyr His Thr Lys Gly Asp His Glu Val
115 120 125

Lys Ala Glu Gln Val Lys Ala Ser Lys Glu Met Gly Glu Thr Leu Leu
130 135 140

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
145 150 155

<210> SEQ ID NO 35
 <211> LENGTH: 159
 <212> TYPE: PRT
 <213> ORGANISM: Betula verrucosa (White birch) (Betula pendula)

<400> SEQUENCE: 35

Gly Val Phe Asn Tyr Glu Ser Glu Thr Thr Ser Val Ile Pro Ala Ala
1 5 10 15

Arg Leu Phe Lys Ala Phe Ile Leu Glu Gly Asp Thr Leu Ile Pro Lys
20 25 30

Val Ala Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly
35 40 45

Gly Pro Gly Thr Ile Lys Lys Ile Thr Phe Pro Glu Gly Ser Pro Phe
50 55 60

Lys Tyr Val Lys Glu Arg Val Asp Glu Val Asp His Ala Asn Phe Lys
65 70 75 80

Tyr Ser Tyr Ser Met Ile Glu Gly Gly Ala Leu Gly Asp Thr Leu Glu
85 90 95

Lys Ile Cys Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly Gly Ser
100 105 110

Ile Leu Lys Ile Ser Asn Lys Tyr His Thr Lys Gly Asp Gln Glu Met
115 120 125

Lys Ala Glu His Met Lys Ala Ile Lys Glu Lys Gly Glu Ala Leu Leu
130 135 140

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
145 150 155

<210> SEQ ID NO 36
 <211> LENGTH: 159
 <212> TYPE: PRT
 <213> ORGANISM: Betula verrucosa (White birch) (Betula pendula)

<400> SEQUENCE: 36

Gly Val Phe Asn Tyr Glu Ile Glu Thr Thr Ser Val Ile Pro Ala Ala
1 5 10 15

Arg Leu Phe Lys Ala Phe Ile Leu Asp Gly Asp Asn Leu Val Pro Lys
20 25 30

Val Ala Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly
35 40 45

Gly Pro Gly Thr Ile Lys Lys Ile Asn Phe Pro Glu Gly Phe Pro Phe
50 55 60

Lys Tyr Val Lys Asp Arg Val Asp Glu Val Asp His Thr Asn Phe Lys
65 70 75 80

Tyr Asn Tyr Ser Val Ile Glu Gly Gly Pro Val Gly Asp Thr Leu Glu
85 90 95

-continued

Lys Ile Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly Gly Cys
 100 105 110

Val Leu Lys Ile Ser Asn Lys Tyr His Thr Lys Gly Asn His Glu Val
 115 120 125

Lys Ala Glu Gln Val Lys Ala Ser Lys Glu Met Gly Glu Thr Leu Leu
 130 135 140

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
 145 150 155

<210> SEQ ID NO 37
 <211> LENGTH: 159
 <212> TYPE: PRT
 <213> ORGANISM: Betula verrucosa (White birch) (Betula pendula)

<400> SEQUENCE: 37

Gly Val Phe Asn Tyr Glu Thr Glu Ala Thr Ser Val Ile Pro Ala Ala
 1 5 10 15

Arg Leu Phe Lys Ala Phe Ile Leu Asp Gly Asp Asn Leu Phe Pro Lys
 20 25 30

Val Ala Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly
 35 40 45

Gly Pro Gly Thr Ile Lys Lys Ile Ser Phe Pro Glu Gly Ile Pro Phe
 50 55 60

Lys Tyr Val Lys Gly Arg Val Asp Glu Val Asp His Thr Asn Phe Lys
 65 70 75 80

Tyr Ser Tyr Ser Val Ile Glu Gly Gly Pro Val Gly Asp Thr Leu Glu
 85 90 95

Lys Ile Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asn Gly Gly Ser
 100 105 110

Ile Leu Lys Ile Asn Asn Lys Tyr His Thr Lys Gly Asp His Glu Val
 115 120 125

Lys Ala Glu Gln Ile Lys Ala Ser Lys Glu Met Gly Glu Thr Leu Leu
 130 135 140

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
 145 150 155

<210> SEQ ID NO 38
 <211> LENGTH: 159
 <212> TYPE: PRT
 <213> ORGANISM: Betula verrucosa (White birch) (Betula pendula)

<400> SEQUENCE: 38

Gly Val Phe Asn Tyr Glu Ile Glu Ala Thr Ser Val Ile Pro Ala Ala
 1 5 10 15

Arg Leu Phe Lys Ala Phe Ile Leu Asp Gly Asp Asn Leu Phe Pro Lys
 20 25 30

Val Ala Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly
 35 40 45

Gly Pro Gly Thr Ile Lys Lys Ile Ser Phe Pro Glu Gly Phe Pro Phe
 50 55 60

Lys Tyr Val Lys Asp Arg Val Asp Glu Val Asp His Thr Asn Phe Lys
 65 70 75 80

Tyr Ser Tyr Ser Val Ile Glu Gly Gly Pro Val Gly Asp Thr Leu Glu
 85 90 95

Lys Ile Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asn Gly Gly Ser
 100 105 110

-continued

Ile Leu Lys Ile Asn Asn Lys Tyr His Thr Lys Gly Asp His Glu Val
 115 120 125

Lys Ala Glu Gln Ile Lys Ala Ser Lys Glu Met Gly Glu Thr Leu Leu
 130 135 140

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
 145 150 155

<210> SEQ ID NO 39
 <211> LENGTH: 159
 <212> TYPE: PRT
 <213> ORGANISM: Betula verrucosa (White birch) (Betula pendula)

<400> SEQUENCE: 39

Gly Val Phe Asn Tyr Glu Ser Glu Thr Thr Ser Val Ile Pro Ala Ala
 1 5 10 15

Arg Leu Phe Lys Ala Phe Ile Leu Glu Gly Asp Asn Leu Ile Pro Lys
 20 25 30

Val Ala Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly
 35 40 45

Gly Pro Gly Thr Ile Lys Lys Ile Asn Phe Pro Glu Gly Phe Pro Phe
 50 55 60

Lys Tyr Val Lys Asp Arg Val Asp Glu Val Asp His Thr Asn Phe Lys
 65 70 75 80

Tyr Asn Tyr Ser Val Ile Glu Gly Gly Pro Val Gly Asp Thr Leu Glu
 85 90 95

Lys Ile Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly Gly Cys
 100 105 110

Val Leu Lys Ile Ser Asn Lys Tyr His Thr Lys Gly Asn His Glu Val
 115 120 125

Lys Ala Glu Gln Val Lys Ala Ser Lys Glu Met Gly Glu Thr Leu Leu
 130 135 140

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
 145 150 155

<210> SEQ ID NO 40
 <211> LENGTH: 159
 <212> TYPE: PRT
 <213> ORGANISM: Betula verrucosa (White birch) (Betula pendula)

<400> SEQUENCE: 40

Gly Val Phe Asn Tyr Glu Thr Glu Ala Thr Ser Val Ile Pro Ala Ala
 1 5 10 15

Arg Leu Phe Lys Ala Phe Ile Leu Asp Gly Asp Asn Leu Phe Pro Lys
 20 25 30

Val Ala Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly
 35 40 45

Gly Pro Gly Thr Ile Lys Lys Ile Ser Phe Pro Glu Gly Phe Pro Phe
 50 55 60

Lys Tyr Val Lys Asp Arg Val Asp Glu Val Asp His Thr Asn Phe Lys
 65 70 75 80

Tyr Ser Tyr Ser Val Ile Glu Gly Gly Pro Val Gly Asp Thr Leu Glu
 85 90 95

Lys Ile Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asn Gly Gly Ser
 100 105 110

Ile Leu Lys Ile Asn Asn Lys Tyr His Thr Lys Gly Asp His Glu Val
 115 120 125

-continued

Lys Ala Glu Gln Ile Lys Ala Ser Lys Glu Met Gly Glu Thr Leu Leu
 130 135 140

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
 145 150 155

<210> SEQ ID NO 41

<211> LENGTH: 159

<212> TYPE: PRT

<213> ORGANISM: Betula verrucosa (White birch) (Betula pendula)

<400> SEQUENCE: 41

Gly Val Phe Asn Tyr Glu Ser Glu Thr Thr Ser Val Ile Pro Ala Ala
 1 5 10 15

Arg Leu Phe Lys Ala Phe Ile Leu Glu Gly Asp Thr Leu Ile Pro Lys
 20 25 30

Val Ala Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly
 35 40 45

Gly Pro Gly Thr Ile Lys Lys Ile Thr Phe Pro Glu Gly Ser Pro Phe
 50 55 60

Lys Tyr Val Lys Glu Arg Val Asp Glu Val Asp His Ala Asn Phe Lys
 65 70 75 80

Tyr Ser Tyr Ser Met Ile Glu Gly Gly Ala Leu Gly Asp Thr Leu Glu
 85 90 95

Lys Ile Cys Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly Gly Ser
 100 105 110

Ile Leu Lys Ile Ser Asn Lys Tyr His Thr Lys Gly Asp His Glu Met
 115 120 125

Lys Ala Glu His Met Lys Ala Ile Lys Glu Lys Gly Glu Ala Leu Leu
 130 135 140

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
 145 150 155

<210> SEQ ID NO 42

<211> LENGTH: 159

<212> TYPE: PRT

<213> ORGANISM: Betula verrucosa (White birch) (Betula pendula)

<400> SEQUENCE: 42

Gly Val Phe Asn Tyr Glu Thr Glu Ala Thr Ser Val Ile Pro Ala Ala
 1 5 10 15

Arg Met Phe Lys Ala Phe Ile Leu Asp Gly Asp Lys Leu Val Pro Lys
 20 25 30

Val Ala Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly
 35 40 45

Gly Pro Gly Thr Ile Lys Lys Ile Asn Phe Pro Glu Gly Phe Pro Phe
 50 55 60

Lys Tyr Val Lys Asp Arg Val Asp Glu Val Asp His Thr Asn Phe Lys
 65 70 75 80

Tyr Asn Tyr Ser Val Ile Glu Gly Gly Pro Val Gly Asp Thr Leu Glu
 85 90 95

Lys Ile Ser Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly Gly Cys
 100 105 110

Val Leu Lys Ile Ser Asn Lys Tyr His Thr Lys Gly Asn His Glu Val
 115 120 125

Lys Ala Glu Gln Val Lys Ala Ser Lys Glu Met Gly Glu Thr Leu Leu
 130 135 140

-continued

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
145 150 155

<210> SEQ ID NO 43
<211> LENGTH: 159
<212> TYPE: PRT
<213> ORGANISM: Betula verrucosa (White birch) (Betula pendula)

<400> SEQUENCE: 43

Gly Val Phe Asn Tyr Glu Ser Glu Thr Thr Ser Val Ile Pro Ala Ala
1 5 10 15
Arg Leu Phe Lys Ala Phe Ile Leu Asp Gly Asp Asn Leu Ile Pro Lys
20 25 30
Val Ala Pro Gln Ala Ile Ser Ser Val Glu Asn Ile Glu Gly Asn Gly
35 40 45
Gly Pro Gly Thr Ile Lys Lys Ile Thr Phe Pro Glu Gly Ser Pro Phe
50 55 60
Lys Tyr Val Lys Glu Arg Val Asp Glu Val Asp His Ala Asn Phe Lys
65 70 75 80
Tyr Ser Tyr Ser Met Ile Glu Gly Gly Ala Leu Gly Asp Thr Leu Glu
85 90 95
Lys Ile Cys Asn Glu Ile Lys Ile Val Ala Thr Pro Asp Gly Gly Ser
100 105 110
Ile Leu Lys Ile Ser Asn Lys Tyr His Thr Lys Gly Asp His Glu Met
115 120 125
Lys Ala Glu His Met Lys Ala Ile Lys Glu Lys Gly Glu Ala Leu Leu
130 135 140
Arg Ala Val Glu Ser Tyr Leu Leu Ala His Ser Asp Ala Tyr Asn
145 150 155

<210> SEQ ID NO 44
<211> LENGTH: 133
<212> TYPE: PRT
<213> ORGANISM: Betula verrucosa (White birch) (Betula pendula)

<400> SEQUENCE: 44

Met Ser Trp Gln Thr Tyr Val Asp Glu His Leu Met Cys Asp Ile Asp
1 5 10 15
Gly Gln Ala Ser Asn Ser Leu Ala Ser Ala Ile Val Gly His Asp Gly
20 25 30
Ser Val Trp Ala Gln Ser Ser Ser Phe Pro Gln Phe Lys Pro Gln Glu
35 40 45
Ile Thr Gly Ile Met Lys Asp Phe Glu Glu Pro Gly His Leu Ala Pro
50 55 60
Thr Gly Leu His Leu Gly Gly Ile Lys Tyr Met Val Ile Gln Gly Glu
65 70 75 80
Ala Gly Ala Val Ile Arg Gly Lys Lys Gly Ser Gly Gly Ile Thr Ile
85 90 95
Lys Lys Thr Gly Gln Ala Leu Val Phe Gly Ile Tyr Glu Glu Pro Val
100 105 110
Thr Pro Gly Gln Cys Asn Met Val Val Glu Arg Leu Gly Asp Tyr Leu
115 120 125
Ile Asp Gln Gly Leu
130

<210> SEQ ID NO 45
<211> LENGTH: 205

-continued

<212> TYPE: PRT

<213> ORGANISM: *Betula verrucosa* (White birch) (*Betula pendula*)

<400> SEQUENCE: 45

Met Pro Cys Ser Thr Glu Ala Met Glu Lys Ala Gly His Gly His Ala
 1 5 10 15

Ser Thr Pro Arg Lys Arg Ser Leu Ser Asn Ser Ser Phe Arg Leu Arg
 20 25 30

Ser Glu Ser Leu Asn Thr Leu Arg Leu Arg Arg Ile Phe Asp Leu Phe
 35 40 45

Asp Lys Asn Ser Asp Gly Ile Ile Thr Val Asp Glu Leu Ser Arg Ala
 50 55 60

Leu Asn Leu Leu Gly Leu Glu Thr Asp Leu Ser Glu Leu Glu Ser Thr
 65 70 75 80

Val Lys Ser Phe Thr Arg Glu Gly Asn Ile Gly Leu Gln Phe Glu Asp
 85 90 95

Phe Ile Ser Leu His Gln Ser Leu Asn Asp Ser Tyr Phe Ala Tyr Gly
 100 105 110

Gly Glu Asp Glu Asp Asp Asn Glu Glu Asp Met Arg Lys Ser Ile Leu
 115 120 125

Ser Gln Glu Glu Ala Asp Ser Phe Gly Gly Phe Lys Val Phe Asp Glu
 130 135 140

Asp Gly Asp Gly Tyr Ile Ser Ala Arg Glu Leu Gln Met Val Leu Gly
 145 150 155 160

Lys Leu Gly Phe Ser Glu Gly Ser Glu Ile Asp Arg Val Glu Lys Met
 165 170 175

Ile Val Ser Val Asp Ser Asn Arg Asp Gly Arg Val Asp Phe Phe Glu
 180 185 190

Phe Lys Asp Met Met Arg Ser Val Leu Val Arg Ser Ser
 195 200 205

<210> SEQ ID NO 46

<211> LENGTH: 352

<212> TYPE: PRT

<213> ORGANISM: *Blattella germanica* (German cockroach)

<400> SEQUENCE: 46

Met Ile Gly Leu Lys Leu Val Thr Val Leu Phe Ala Val Ala Thr Ile
 1 5 10 15

Thr His Ala Ala Glu Leu Gln Arg Val Pro Leu Tyr Lys Leu Val His
 20 25 30

Val Phe Ile Asn Thr Gln Tyr Ala Gly Ile Thr Lys Ile Gly Asn Gln
 35 40 45

Asn Phe Leu Thr Val Phe Asp Ser Thr Ser Cys Asn Val Val Val Ala
 50 55 60

Ser Gln Glu Cys Val Gly Gly Ala Cys Val Cys Pro Asn Leu Gln Lys
 65 70 75 80

Tyr Glu Lys Leu Lys Pro Lys Tyr Ile Ser Asp Gly Asn Val Gln Val
 85 90 95

Lys Phe Phe Asp Thr Gly Ser Ala Val Gly Arg Gly Ile Glu Asp Ser
 100 105 110

Leu Thr Ile Ser Asn Leu Thr Thr Ser Gln Gln Asp Ile Val Leu Ala
 115 120 125

Asp Glu Leu Ser Gln Glu Val Cys Ile Leu Ser Ala Asp Val Val Val
 130 135 140

-continued

Gly Ile Ala Ala Pro Gly Cys Pro Asn Ala Leu Lys Gly Lys Thr Val
 145 150 155 160
 Leu Glu Asn Phe Val Glu Glu Asn Leu Ile Ala Pro Val Phe Ser Ile
 165 170 175
 His His Ala Arg Phe Gln Asp Gly Glu His Phe Gly Glu Ile Ile Phe
 180 185 190
 Gly Gly Ser Asp Trp Lys Tyr Val Asp Gly Glu Phe Thr Tyr Val Pro
 195 200 205
 Leu Val Gly Asp Asp Ser Trp Lys Phe Arg Leu Asp Gly Val Lys Ile
 210 215 220
 Gly Asp Thr Thr Val Ala Pro Ala Gly Thr Gln Ala Ile Ile Asp Thr
 225 230 235 240
 Ser Lys Ala Ile Ile Val Gly Pro Lys Ala Tyr Val Asn Pro Ile Asn
 245 250 255
 Glu Ala Ile Gly Cys Val Val Glu Lys Thr Thr Thr Arg Arg Ile Cys
 260 265 270
 Lys Leu Asp Cys Ser Lys Ile Pro Ser Leu Pro Asp Val Thr Phe Val
 275 280 285
 Ile Asn Gly Arg Asn Phe Asn Ile Ser Ser Gln Tyr Tyr Ile Gln Gln
 290 295 300
 Asn Gly Asn Leu Cys Tyr Ser Gly Phe Gln Pro Cys Gly His Ser Asp
 305 310 315 320
 His Phe Phe Ile Gly Asp Phe Phe Val Asp His Tyr Tyr Ser Glu Phe
 325 330 335
 Asn Trp Glu Asn Lys Thr Met Gly Phe Gly Arg Ser Val Glu Ser Val
 340 345 350

<210> SEQ ID NO 47

<211> LENGTH: 182

<212> TYPE: PRT

<213> ORGANISM: Blattella germanica (German cockroach)

<400> SEQUENCE: 47

Ala Val Leu Ala Leu Cys Ala Thr Asp Thr Leu Ala Asn Glu Asp Cys
 1 5 10 15
 Phe Arg His Glu Ser Leu Val Pro Asn Leu Asp Tyr Glu Arg Phe Arg
 20 25 30
 Gly Ser Trp Ile Ile Ala Ala Gly Thr Ser Glu Ala Leu Thr Gln Tyr
 35 40 45
 Lys Cys Trp Ile Asp Arg Phe Ser Tyr Asp Asp Ala Leu Val Ser Lys
 50 55 60
 Tyr Thr Asp Ser Gln Gly Lys Asn Arg Thr Thr Ile Arg Gly Arg Thr
 65 70 75 80
 Lys Phe Glu Gly Asn Lys Phe Thr Ile Asp Tyr Asn Asp Lys Gly Lys
 85 90 95
 Ala Phe Ser Ala Pro Tyr Ser Val Leu Ala Thr Asp Tyr Glu Asn Tyr
 100 105 110
 Ala Ile Val Glu Gly Cys Pro Ala Ala Ala Asn Gly His Val Ile Tyr
 115 120 125
 Val Gln Ile Arg Phe Ser Val Arg Arg Phe His Pro Lys Leu Gly Asp
 130 135 140
 Lys Glu Met Ile Gln His Tyr Thr Leu Asp Gln Val Asn Gln His Lys
 145 150 155 160
 Lys Ala Ile Glu Glu Asp Leu Lys His Phe Asn Leu Lys Tyr Glu Asp
 165 170 175

-continued

Leu His Ser Thr Cys His
180

<210> SEQ ID NO 48
<211> LENGTH: 203
<212> TYPE: PRT
<213> ORGANISM: *Blattella germanica* (German cockroach)

<400> SEQUENCE: 48

Ala Pro Ser Tyr Lys Leu Thr Tyr Cys Pro Val Lys Ala Leu Gly Glu
1 5 10 15
Pro Ile Arg Phe Leu Leu Ser Tyr Gly Glu Lys Asp Phe Glu Asp Tyr
20 25 30
Arg Phe Gln Glu Gly Asp Trp Pro Asn Leu Lys Pro Ser Met Pro Phe
35 40 45
Gly Lys Thr Pro Val Leu Glu Ile Asp Gly Lys Gln Thr His Gln Ser
50 55 60
Val Ala Ile Ser Arg Tyr Leu Gly Lys Gln Phe Gly Leu Ser Gly Lys
65 70 75 80
Asp Asp Trp Glu Asn Leu Glu Ile Asp Met Ile Val Asp Thr Ile Ser
85 90 95
Asp Phe Arg Ala Ala Ile Ala Asn Tyr His Tyr Asp Ala Asp Glu Asn
100 105 110
Ser Lys Gln Lys Lys Trp Asp Pro Leu Lys Lys Glu Thr Ile Pro Tyr
115 120 125
Tyr Thr Lys Lys Phe Asp Glu Val Val Lys Ala Asn Gly Gly Tyr Leu
130 135 140
Ala Ala Gly Lys Leu Thr Trp Ala Asp Phe Tyr Phe Val Ala Ile Leu
145 150 155 160
Asp Tyr Leu Asn His Met Ala Lys Glu Asp Leu Val Ala Asn Gln Pro
165 170 175
Asn Leu Lys Ala Leu Arg Glu Lys Val Leu Gly Leu Pro Ala Ile Lys
180 185 190
Ala Trp Val Ala Lys Arg Pro Pro Thr Asp Leu
195 200

<210> SEQ ID NO 49
<211> LENGTH: 144
<212> TYPE: PRT
<213> ORGANISM: *Blomia tropicalis* (Mite)

<400> SEQUENCE: 49

Met Lys Ser Val Leu Ile Phe Leu Val Ala Ile Ala Leu Phe Ser Ala
1 5 10 15
Asn Ile Val Ser Ala Asp Glu Gln Thr Thr Arg Gly Arg His Thr Glu
20 25 30
Pro Asp Asp His His Glu Lys Pro Thr Thr Gln Cys Thr His Glu Glu
35 40 45
Thr Thr Ser Thr Gln His His His Glu Glu Val Val Thr Thr Gln Thr
50 55 60
Pro His His Glu Glu Lys Thr Thr Thr Glu Glu Thr His His Ser Asp
65 70 75 80
Asp Leu Ile Val His Glu Gly Gly Lys Thr Tyr His Val Val Cys His
85 90 95
Glu Glu Gly Pro Ile His Ile Gln Glu Met Cys Asn Lys Tyr Ile Ile
100 105 110

-continued

Cys Ser Lys Ser Gly Ser Leu Trp Tyr Ile Thr Val Met Pro Cys Ser
 115 120 125

Ile Gly Thr Lys Phe Asp Pro Ile Ser Arg Asn Cys Val Leu Asp Asn
 130 135 140

<210> SEQ ID NO 50

<211> LENGTH: 172

<212> TYPE: PRT

<213> ORGANISM: Bos taurus (Bovine)

<400> SEQUENCE: 50

Met Lys Ala Val Phe Leu Thr Leu Leu Phe Gly Leu Val Cys Thr Ala
 1 5 10 15

Gln Glu Thr Pro Ala Glu Ile Asp Pro Ser Lys Ile Pro Gly Glu Trp
 20 25 30

Arg Ile Ile Tyr Ala Ala Ala Asp Asn Lys Asp Lys Ile Val Glu Gly
 35 40 45

Gly Pro Leu Arg Asn Tyr Tyr Arg Arg Ile Glu Cys Ile Asn Asp Cys
 50 55 60

Glu Ser Leu Ser Ile Thr Phe Tyr Leu Lys Asp Gln Gly Thr Cys Leu
 65 70 75 80

Leu Leu Thr Glu Val Ala Lys Arg Gln Glu Gly Tyr Val Tyr Val Leu
 85 90 95

Glu Phe Tyr Gly Thr Asn Thr Leu Glu Val Ile His Val Ser Glu Asn
 100 105 110

Met Leu Val Thr Tyr Val Glu Asn Tyr Asp Gly Glu Arg Ile Thr Lys
 115 120 125

Met Thr Glu Gly Leu Ala Lys Gly Thr Ser Phe Thr Pro Glu Glu Leu
 130 135 140

Glu Lys Tyr Gln Gln Leu Asn Ser Glu Arg Gly Val Pro Asn Glu Asn
 145 150 155 160

Ile Glu Asn Leu Ile Lys Thr Asp Asn Cys Pro Pro
 165 170

<210> SEQ ID NO 51

<211> LENGTH: 178

<212> TYPE: PRT

<213> ORGANISM: Bos taurus (Bovine)

<400> SEQUENCE: 51

Met Lys Cys Leu Leu Leu Ala Leu Ala Leu Thr Cys Gly Ala Gln Ala
 1 5 10 15

Leu Ile Val Thr Gln Thr Met Lys Gly Leu Asp Ile Gln Lys Val Ala
 20 25 30

Gly Thr Trp Tyr Ser Leu Ala Met Ala Ala Ser Asp Ile Ser Leu Leu
 35 40 45

Asp Ala Gln Ser Ala Pro Leu Arg Val Tyr Val Glu Glu Leu Lys Pro
 50 55 60

Thr Pro Glu Gly Asp Leu Glu Ile Leu Leu Gln Lys Trp Glu Asn Gly
 65 70 75 80

Glu Cys Ala Gln Lys Lys Ile Ile Ala Glu Lys Thr Lys Ile Pro Ala
 85 90 95

Val Phe Lys Ile Asp Ala Leu Asn Glu Asn Lys Val Leu Val Leu Asp
 100 105 110

Thr Asp Tyr Lys Lys Tyr Leu Leu Phe Cys Met Glu Asn Ser Ala Glu
 115 120 125

-continued

Pro Glu Gln Ser Leu Ala Cys Gln Cys Leu Val Arg Thr Pro Glu Val
 130 135 140

Asp Asp Glu Ala Leu Glu Lys Phe Asp Lys Ala Leu Lys Ala Leu Pro
 145 150 155 160

Met His Ile Arg Leu Ser Phe Asn Pro Thr Gln Leu Glu Glu Gln Cys
 165 170 175

His Ile

<210> SEQ ID NO 52

<211> LENGTH: 129

<212> TYPE: PRT

<213> ORGANISM: Brassica juncea (Leaf mustard) (Indian mustard)

<400> SEQUENCE: 52

Ala Gly Pro Phe Arg Phe Pro Arg Cys Arg Lys Glu Phe Gln Gln Ala
 1 5 10 15

Gln His Leu Arg Ala Cys Gln Gln Trp Leu His Lys Gln Ala Met Gln
 20 25 30

Ser Gly Ser Gly Pro Gln Pro Gln Gly Pro Gln Gln Arg Pro Pro Leu
 35 40 45

Leu Gln Gln Cys Cys Asn Glu Leu His Gln Glu Glu Pro Leu Cys Val
 50 55 60

Cys Pro Thr Leu Lys Gly Ala Ser Lys Ala Val Lys Gln Gln Ile Arg
 65 70 75 80

Gln Gln Gly Gln Gln Gln Gly Gln Gln Gly Gln Gln Leu Gln His Glu
 85 90 95

Ile Ser Arg Ile Tyr Gln Thr Ala Thr His Leu Pro Arg Val Cys Asn
 100 105 110

Ile Pro Arg Val Ser Ile Cys Pro Phe Gln Lys Thr Met Pro Gly Pro
 115 120 125

Ser

<210> SEQ ID NO 53

<211> LENGTH: 350

<212> TYPE: PRT

<213> ORGANISM: Candida albicans (Yeast)

<400> SEQUENCE: 53

Met Ser Glu Gln Ile Pro Lys Thr Gln Lys Ala Val Val Phe Asp Thr
 1 5 10 15

Asn Gly Gly Gln Leu Val Tyr Lys Asp Tyr Pro Val Pro Thr Pro Lys
 20 25 30

Pro Asn Glu Leu Leu Ile His Val Lys Tyr Ser Gly Val Cys His Thr
 35 40 45

Asp Leu His Ala Arg Lys Gly Asp Trp Pro Leu Ala Thr Lys Leu Pro
 50 55 60

Leu Val Gly Gly His Glu Gly Ala Gly Val Val Val Gly Met Gly Glu
 65 70 75 80

Asn Val Lys Gly Trp Lys Ile Gly Asp Phe Ala Gly Ile Lys Trp Leu
 85 90 95

Asn Gly Ser Cys Met Ser Cys Glu Phe Cys Gln Gln Gly Ala Glu Pro
 100 105 110

Asn Cys Gly Glu Ala Asp Leu Ser Gly Tyr Thr His Asp Gly Ser Phe
 115 120 125

Glu Gln Tyr Ala Thr Ala Asp Ala Val Gln Ala Ala Lys Ile Pro Ala

-continued

130	135	140
Gly Thr Asp Leu Ala Asn Val Ala Pro Ile Leu Cys Ala Gly Val Thr 145	150	155
Val Tyr Lys Ala Leu Lys Thr Ala Asp Leu Ala Ala Gly Gln Trp Val 165	170	175
Ala Ile Ser Gly Ala Gly Gly Gly Leu Gly Ser Leu Ala Val Gln Tyr 180	185	190
Ala Arg Ala Met Gly Leu Arg Val Val Ala Ile Asp Gly Gly Asp Glu 195	200	205
Lys Gly Glu Phe Val Lys Ser Leu Gly Ala Glu Ala Tyr Val Asp Phe 210	215	220
Thr Lys Asp Lys Asp Ile Val Glu Ala Val Lys Lys Ala Thr Asp Gly 225	230	235
Gly Pro His Gly Ala Ile Asn Val Ser Val Ser Glu Lys Ala Ile Asp 245	250	255
Gln Ser Val Glu Tyr Val Arg Pro Leu Gly Lys Val Val Leu Val Gly 260	265	270
Leu Pro Ala His Ala Lys Val Thr Ala Pro Val Phe Asp Ala Val Val 275	280	285
Lys Ser Ile Glu Ile Lys Gly Ser Tyr Val Gly Asn Arg Lys Asp Thr 290	295	300
Ala Glu Ala Ile Asp Phe Phe Ser Arg Gly Leu Ile Lys Cys Pro Ile 305	310	315
Lys Ile Val Gly Leu Ser Asp Leu Pro Glu Val Phe Lys Leu Met Glu 325	330	335
Glu Gly Lys Ile Leu Gly Arg Tyr Val Leu Asp Thr Ser Lys 340	345	350

<210> SEQ ID NO 54

<211> LENGTH: 174

<212> TYPE: PRT

<213> ORGANISM: Canis familiaris (Dog)

<400> SEQUENCE: 54

Met Lys Thr Leu Leu Leu Thr Ile Gly Phe Ser Leu Ile Ala Ile Leu 1	5	10	15
Gln Ala Gln Asp Thr Pro Ala Leu Gly Lys Asp Thr Val Ala Val Ser 20	25	30	
Gly Lys Trp Tyr Leu Lys Ala Met Thr Ala Asp Gln Glu Val Pro Glu 35	40	45	
Lys Pro Asp Ser Val Thr Pro Met Ile Leu Lys Ala Gln Lys Gly Gly 50	55	60	
Asn Leu Glu Ala Lys Ile Thr Met Leu Thr Asn Gly Gln Cys Gln Asn 65	70	75	80
Ile Thr Val Val Leu His Lys Thr Ser Glu Pro Gly Lys Tyr Thr Ala 85	90	95	
Tyr Glu Gly Gln Arg Val Val Phe Ile Gln Pro Ser Pro Val Arg Asp 100	105	110	
His Tyr Ile Leu Tyr Cys Glu Gly Glu Leu His Gly Arg Gln Ile Arg 115	120	125	
Met Ala Lys Leu Leu Gly Arg Asp Pro Glu Gln Ser Gln Glu Ala Leu 130	135	140	
Glu Asp Phe Arg Glu Phe Ser Arg Ala Lys Gly Leu Asn Gln Glu Ile 145	150	155	160

-continued

Leu Glu Leu Ala Gln Ser Glu Thr Cys Ser Pro Gly Gly Gln
 165 170

<210> SEQ ID NO 55
 <211> LENGTH: 180
 <212> TYPE: PRT
 <213> ORGANISM: Canis familiaris (Dog)

<400> SEQUENCE: 55

Met Gln Leu Leu Leu Leu Thr Val Gly Leu Ala Leu Ile Cys Gly Leu
 1 5 10 15
 Gln Ala Gln Glu Gly Asn His Glu Glu Pro Gln Gly Gly Leu Glu Glu
 20 25 30
 Leu Ser Gly Arg Trp His Ser Val Ala Leu Ala Ser Asn Lys Ser Asp
 35 40 45
 Leu Ile Lys Pro Trp Gly His Phe Arg Val Phe Ile His Ser Met Ser
 50 55 60
 Ala Lys Asp Gly Asn Leu His Gly Asp Ile Leu Ile Pro Gln Asp Gly
 65 70 75 80
 Gln Cys Glu Lys Val Ser Leu Thr Ala Phe Lys Thr Ala Thr Ser Asn
 85 90 95
 Lys Phe Asp Leu Glu Tyr Trp Gly His Asn Asp Leu Tyr Leu Ala Glu
 100 105 110
 Val Asp Pro Lys Ser Tyr Leu Ile Leu Tyr Met Ile Asn Gln Tyr Asn
 115 120 125
 Asp Asp Thr Ser Leu Val Ala His Leu Met Val Arg Asp Leu Ser Arg
 130 135 140
 Gln Gln Asp Phe Leu Pro Ala Phe Glu Ser Val Cys Glu Asp Ile Gly
 145 150 155 160
 Leu His Lys Asp Gln Ile Val Val Leu Ser Asp Asp Asp Arg Cys Gln
 165 170 175
 Gly Ser Arg Asp
 180

<210> SEQ ID NO 56
 <211> LENGTH: 159
 <212> TYPE: PRT
 <213> ORGANISM: Carpinus betulus (Hornbeam)

<400> SEQUENCE: 56

Gly Val Phe Asn Tyr Glu Ala Glu Thr Pro Ser Val Ile Pro Ala Ala
 1 5 10 15
 Arg Leu Phe Lys Ser Tyr Val Leu Asp Gly Asp Lys Leu Ile Pro Lys
 20 25 30
 Val Ala Pro Gln Val Ile Ser Ser Val Glu Asn Val Gly Gly Asn Gly
 35 40 45
 Gly Pro Gly Thr Ile Lys Asn Ile Thr Phe Ala Glu Gly Ile Pro Phe
 50 55 60
 Lys Phe Val Lys Glu Arg Val Asp Glu Val Asp Asn Ala Asn Phe Lys
 65 70 75 80
 Tyr Asn Tyr Thr Val Ile Glu Gly Asp Val Leu Gly Asp Lys Leu Glu
 85 90 95
 Lys Val Ser His Glu Leu Lys Ile Val Ala Ala Pro Gly Gly Gly Ser
 100 105 110
 Ile Val Lys Ile Ser Ser Lys Phe His Ala Lys Gly Tyr His Glu Val
 115 120 125

-continued

Asn Ala Glu Lys Met Lys Gly Ala Lys Glu Met Ala Glu Lys Leu Leu
 130 135 140

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Thr Ala Glu Tyr Asn
 145 150 155

<210> SEQ ID NO 57

<211> LENGTH: 159

<212> TYPE: PRT

<213> ORGANISM: Carpinus betulus (Hornbeam)

<400> SEQUENCE: 57

Gly Val Phe Asn Tyr Glu Ala Glu Thr Thr Ser Val Ile Pro Ala Ala
 1 5 10 15

Arg Leu Phe Lys Ala Phe Ile Leu Asp Gly Asn Lys Leu Ile Pro Lys
 20 25 30

Val Ser Pro Gln Ala Val Ser Ser Val Glu Asn Val Glu Gly Asn Gly
 35 40 45

Gly Pro Gly Thr Ile Lys Lys Ile Thr Phe Ser Glu Gly Ser Pro Val
 50 55 60

Lys Tyr Val Lys Glu Arg Val Glu Glu Ile Asp His Thr Asn Phe Lys
 65 70 75 80

Tyr Asn Tyr Thr Val Ile Glu Gly Asp Val Leu Gly Asp Lys Leu Glu
 85 90 95

Lys Val Ser His Glu Leu Lys Ile Val Ala Ala Pro Gly Gly Gly Ser
 100 105 110

Ile Val Lys Ile Ser Ser Lys Phe His Ala Lys Gly Tyr His Glu Val
 115 120 125

Asn Ala Glu Glu Met Lys Gly Ala Lys Glu Met Ala Glu Lys Leu Leu
 130 135 140

Arg Ala Val Glu Ser Tyr Leu Leu Ala His Thr Ala Glu Tyr Asn
 145 150 155

<210> SEQ ID NO 58

<211> LENGTH: 375

<212> TYPE: PRT

<213> ORGANISM: Chamaecyparis obtusa (Japanese cypress)

<400> SEQUENCE: 58

Met Ala Ser Cys Thr Leu Leu Ala Val Leu Val Phe Leu Cys Ala Ile
 1 5 10 15

Val Ser Cys Phe Ser Asp Asn Pro Ile Asp Ser Cys Trp Arg Gly Asp
 20 25 30

Ala Asn Trp Asp Gln Asn Arg Met Lys Leu Ala Asp Cys Ala Val Gly
 35 40 45

Phe Gly Ser Ser Ala Met Gly Gly Lys Gly Gly Ala Phe Tyr Thr Val
 50 55 60

Thr Ser Ser Asp Asp Asp Pro Val Asn Pro Ala Pro Gly Thr Leu Arg
 65 70 75 80

Tyr Gly Ala Thr Arg Glu Arg Ser Leu Trp Ile Ile Phe Ser Lys Asn
 85 90 95

Leu Asn Ile Lys Leu Asn Met Pro Leu Tyr Ile Ala Gly Asn Lys Thr
 100 105 110

Ile Asp Gly Arg Gly Ala Glu Val His Ile Gly Asn Gly Gly Pro Cys
 115 120 125

Leu Phe Met Arg Thr Val Ser His Val Ile Leu His Gly Leu Asn Ile
 130 135 140

-continued

His Gly Cys Asn Thr Ser Val Ser Gly Asn Val Leu Ile Ser Glu Ala
 145 150 155 160
 Ser Gly Val Val Pro Val His Ala Gln Asp Gly Asp Ala Ile Thr Met
 165 170 175
 Arg Asn Val Thr Asp Val Trp Ile Asp His Asn Ser Leu Ser Asp Ser
 180 185 190
 Ser Asp Gly Leu Val Asp Val Thr Leu Ala Ser Thr Gly Val Thr Ile
 195 200 205
 Ser Asn Asn His Phe Phe Asn His His Lys Val Met Leu Leu Gly His
 210 215 220
 Ser Asp Ile Tyr Ser Asp Asp Lys Ser Met Lys Val Thr Val Ala Phe
 225 230 235 240
 Asn Gln Phe Gly Pro Asn Ala Gly Gln Arg Met Pro Arg Ala Arg Tyr
 245 250 255
 Gly Leu Ile His Val Ala Asn Asn Asn Tyr Asp Pro Trp Ser Ile Tyr
 260 265 270
 Ala Ile Gly Gly Ser Ser Asn Pro Thr Ile Leu Ser Glu Gly Asn Ser
 275 280 285
 Phe Thr Ala Pro Asn Asp Ser Asp Lys Lys Glu Val Thr Arg Arg Val
 290 295 300
 Gly Cys Glu Ser Pro Ser Thr Cys Ala Asn Trp Val Trp Arg Ser Thr
 305 310 315 320
 Gln Asp Ser Phe Asn Asn Gly Ala Tyr Phe Val Ser Ser Gly Lys Asn
 325 330 335
 Glu Gly Thr Asn Ile Tyr Asn Asn Asn Glu Ala Phe Lys Val Glu Asn
 340 345 350
 Gly Ser Ala Ala Pro Gln Leu Thr Lys Asn Ala Gly Val Leu Thr Cys
 355 360 365
 Ile Leu Ser Lys Pro Cys Ser
 370 375

<210> SEQ ID NO 59
 <211> LENGTH: 496
 <212> TYPE: PRT
 <213> ORGANISM: Cladosporium herbarum

<400> SEQUENCE: 59

Met Thr Ser Val Gln Leu Glu Thr Pro His Ser Gly Lys Tyr Glu Gln
 1 5 10 15
 Pro Thr Gly Leu Phe Ile Asn Asn Glu Phe Val Lys Gly Gln Glu Gly
 20 25 30
 Lys Thr Phe Asp Val Ile Asn Pro Ser Asp Glu Ser Val Ile Thr Gln
 35 40 45
 Val His Glu Ala Thr Glu Lys Asp Val Asp Ile Ala Val Ala Ala Ala
 50 55 60
 Arg Gln Ala Phe Glu Gly Ser Trp Arg Leu Glu Thr Pro Glu Asn Arg
 65 70 75 80
 Gly Lys Leu Leu Asn Asn Leu Ala Asn Leu Phe Glu Lys Asn Thr Asp
 85 90 95
 Leu Leu Ala Ala Val Glu Ser Leu Asp Asn Gly Lys Ala Thr Ser Met
 100 105 110
 Ala Arg Val Thr Ser Ala Cys Ala Ser Gly Cys Leu Arg Tyr Tyr Gly
 115 120 125
 Gly Trp Ala Asp Lys Ile Thr Gly Lys Val Ile Asp Thr Thr Pro Asp
 130 135 140

-continued

Thr Phe Asn Tyr Val Lys Lys Glu Pro Ile Gly Val Cys Arg Ser Asp
 145 150 155 160
 His Ser Leu Glu Leu Pro Leu Leu Met Trp Ala Trp Lys Ile Gly Pro
 165 170 175
 Ala Ile Ala Cys Gly Asn Thr Val Val Leu Lys Thr Ala Glu Gln Thr
 180 185 190
 Pro Leu Gly Gly Leu Val Ala Ala Ser Leu Val Lys Glu Ala Gly Phe
 195 200 205
 Pro Pro Gly Val Ile Asn Val Ile Ser Gly Phe Gly Lys Val Ala Gly
 210 215 220
 Ala Ala Leu Ser Ser His Met Asp Val Asp Lys Val Ala Phe Thr Gly
 225 230 235 240
 Ser Thr Val Val Gly Arg Thr Ile Leu Lys Ala Ala Ala Ser Ser Asn
 245 250 255
 Leu Lys Lys Val Thr Leu Glu Leu Gly Gly Lys Ser Pro Asn Ile Val
 260 265 270
 Phe Glu Asp Ala Asp Ile Asp Asn Ala Ile Ser Trp Val Asn Phe Gly
 275 280 285
 Ile Phe Phe Asn His Gly Gln Cys Cys Cys Ala Gly Ser Arg Val Tyr
 290 295 300
 Val Gln Glu Ser Ile Tyr Asp Lys Phe Val Gln Lys Phe Lys Glu Arg
 305 310 315 320
 Ala Gln Lys Asn Val Val Gly Asp Pro Phe Ala Ala Asp Thr Phe Gln
 325 330 335
 Gly Pro Gln Val Ser Lys Val Gln Phe Asp Arg Ile Met Glu Tyr Ile
 340 345 350
 Gln Ala Gly Lys Asp Ala Gly Ala Thr Val Glu Thr Gly Gly Ser Arg
 355 360 365
 Lys Gly Asp Lys Gly Tyr Phe Ile Glu Pro Thr Ile Phe Ser Asn Val
 370 375 380
 Thr Glu Asp Met Lys Ile Val Lys Glu Glu Ile Phe Gly Pro Val Cys
 385 390 395 400
 Ser Ile Ala Lys Phe Lys Thr Lys Glu Asp Ala Ile Lys Leu Gly Asn
 405 410 415
 Ala Ser Thr Tyr Gly Leu Ala Ala Ala Val His Thr Lys Asn Leu Asn
 420 425 430
 Thr Ala Ile Glu Val Ser Asn Ala Leu Lys Ala Gly Thr Val Trp Val
 435 440 445
 Asn Thr Tyr Asn Thr Leu His His Gln Met Pro Phe Gly Gly Tyr Lys
 450 455 460
 Glu Ser Gly Ile Gly Arg Glu Leu Gly Glu Asp Ala Leu Ala Asn Tyr
 465 470 475 480
 Thr Gln Thr Lys Thr Val Ser Ile Arg Leu Gly Asp Ala Leu Phe Gly
 485 490 495

<210> SEQ ID NO 60

<211> LENGTH: 111

<212> TYPE: PRT

<213> ORGANISM: Cladosporium herbarum

<400> SEQUENCE: 60

Met Lys Tyr Met Ala Ala Tyr Leu Leu Leu Gly Leu Ala Gly Asn Ser
 1 5 10 15

Ser Pro Ser Ala Glu Asp Ile Lys Thr Val Leu Ser Ser Val Gly Ile

-continued

20					25					30					
Asp	Ala	Asp	Glu	Glu	Arg	Leu	Ser	Ser	Leu	Leu	Lys	Glu	Leu	Glu	Gly
	35						40				45				
Lys	Asp	Ile	Asn	Glu	Leu	Ile	Ser	Ser	Gly	Ser	Gln	Lys	Leu	Ala	Ser
	50					55					60				
Val	Pro	Ser	Gly	Gly	Ser	Gly	Ala	Ala	Pro	Ser	Ala	Gly	Gly	Ala	Ala
65					70					75					80
Ala	Ala	Gly	Gly	Ala	Thr	Glu	Ala	Ala	Pro	Glu	Ala	Ala	Lys	Glu	Glu
				85					90					95	
Glu	Lys	Glu	Glu	Ser	Asp	Asp	Asp	Met	Gly	Phe	Gly	Leu	Phe	Asp	
			100					105						110	
<210> SEQ ID NO 61															
<211> LENGTH: 643															
<212> TYPE: PRT															
<213> ORGANISM: Cladosporium herbarum															
<400> SEQUENCE: 61															
Met	Ala	Pro	Ala	Ile	Gly	Ile	Asp	Leu	Gly	Thr	Thr	Tyr	Ser	Cys	Val
1				5					10					15	
Gly	Ile	Tyr	Arg	Asp	Asp	Arg	Ile	Glu	Ile	Ile	Ala	Asn	Asp	Gln	Gly
			20					25					30		
Asn	Arg	Thr	Thr	Pro	Ser	Phe	Val	Ala	Phe	Thr	Asp	Thr	Glu	Arg	Leu
		35					40					45			
Ile	Gly	Asp	Ser	Ala	Lys	Asn	Gln	Val	Ala	Ile	Asn	Pro	His	Asn	Thr
	50					55					60				
Val	Phe	Asp	Ala	Lys	Arg	Leu	Ile	Gly	Arg	Lys	Phe	Gln	Asp	Ala	Glu
65					70					75					80
Val	Gln	Ala	Asp	Met	Lys	His	Phe	Pro	Phe	Lys	Val	Ile	Glu	Lys	Ala
				85					90					95	
Gly	Lys	Pro	Val	Thr	Gln	Val	Glu	Phe	Lys	Gly	Glu	Thr	Lys	Asp	Phe
			100					105						110	
Thr	Pro	Glu	Glu	Ile	Ser	Ser	Met	Ile	Leu	Thr	Lys	Met	Arg	Glu	Thr
		115					120					125			
Ala	Glu	Ser	Tyr	Leu	Gly	Gly	Thr	Val	Asn	Asn	Ala	Val	Ile	Thr	Val
	130					135					140				
Pro	Ala	Tyr	Phe	Asn	Asp	Ser	Gln	Arg	Gln	Ala	Thr	Lys	Asp	Ala	Gly
145					150					155					160
Leu	Ile	Ala	Gly	Leu	Asn	Val	Leu	Arg	Ile	Ile	Asn	Glu	Pro	Thr	Ala
				165					170					175	
Ala	Ala	Ile	Ala	Tyr	Gly	Leu	Asp	Lys	Lys	Gln	Glu	Gly	Glu	Lys	Asn
			180					185					190		
Val	Leu	Ile	Phe	Asp	Leu	Gly	Gly	Gly	Thr	Phe	Asp	Val	Ser	Phe	Leu
		195					200					205			
Thr	Ile	Glu	Glu	Gly	Ile	Phe	Glu	Val	Lys	Ser	Thr	Ala	Gly	Asp	Thr
		210				215						220			
His	Leu	Gly	Gly	Glu	Asp	Phe	Asp	Asn	Arg	Leu	Val	Asn	His	Phe	Ser
225					230					235					240
Asn	Glu	Phe	Lys	Arg	Lys	His	Lys	Lys	Asp	Leu	Ser	Asp	Asn	Ala	Arg
				245					250					255	
Ala	Leu	Arg	Arg	Leu	Arg	Thr	Ala	Cys	Glu	Arg	Ala	Lys	Arg	Thr	Leu
			260					265					270		
Ser	Ser	Ser	Ala	Gln	Thr	Ser	Ile	Glu	Ile	Asp	Ser	Leu	Phe	Glu	Gly
			275				280					285			

-continued

Ile Asp Phe Phe Thr Ser Asn Thr Arg Ala Arg Phe Glu Glu Val Gly
 290 295 300
 Gln Asp Leu Phe Arg Gly Asn Met Glu Pro Gly Glu Arg Thr Leu Arg
 305 310 315 320
 Asp Asp Lys Ile Asp Lys Ser Ser Val His Glu Ile Val Leu Gly Gly
 325 330 335
 Gly Ser Thr Arg Ile Pro Lys Val Gln Lys Leu Val Ser Asp Phe Phe
 340 345 350
 Asn Gly Lys Glu Pro Cys Lys Ser Ile Asn Pro Asp Glu Ala Val Ala
 355 360 365
 Tyr Gly Ala Ala Val Gln Ala Ala Ile Leu Ser Gly Asp Thr Ser Ser
 370 375 380
 Lys Ser Thr Lys Glu Ile Leu Leu Leu Asp Val Ala Pro Leu Ser Leu
 385 390 395 400
 Gly Ile Glu Thr Ala Gly Gly Val Met Thr Ala Leu Ile Lys Arg Asn
 405 410 415
 Thr Thr Ile Pro Thr Lys Lys Ser Glu Thr Phe Ser Thr Phe Ser Asp
 420 425 430
 Asn Gln Pro Gly Val Leu Ile Gln Val Phe Glu Gly Glu Arg Ala Arg
 435 440 445
 Thr Lys Asp Ile Asn Leu Met Gly Lys Phe Glu Leu Ser Gly Ile Arg
 450 455 460
 Pro Ala Pro Arg Gly Val Pro Gln Ile Glu Val Thr Phe Asp Leu Asp
 465 470 475 480
 Ala Asn Gly Ile Met Asn Val Ser Ala Leu Glu Lys Gly Thr Gly Lys
 485 490 495
 Thr Asn Lys Ile Val Ile Thr Asn Asp Lys Gly Arg Leu Ser Lys Glu
 500 505 510
 Glu Ile Glu Arg Met Leu Ala Asp Ala Glu Lys Tyr Lys Glu Glu Asp
 515 520 525
 Glu Ala Glu Ala Gly Arg Ile Gln Ala Lys Asn Gly Leu Glu Ser Tyr
 530 535 540
 Ala Tyr Ser Leu Lys Asn Thr Val Ser Asp Pro Lys Val Glu Glu Lys
 545 550 555 560
 Leu Ser Ala Glu Asp Lys Glu Thr Leu Thr Gly Ala Ile Asp Lys Thr
 565 570 575
 Val Ala Trp Ile Asp Glu Asn Gln Thr Ala Thr Lys Glu Glu Tyr Glu
 580 585 590
 Ala Glu Gln Lys Gln Leu Glu Ser Val Ala Asn Pro Val Met Met Lys
 595 600 605
 Ile Tyr Gly Ala Glu Gly Gly Ala Pro Gly Gly Met Pro Gly Gln Gly
 610 615 620
 Ala Gly Ala Pro Pro Pro Gly Ala Gly Asp Asp Gly Pro Thr Val Glu
 625 630 635 640
 Glu Val Asp

<210> SEQ ID NO 62

<211> LENGTH: 112

<212> TYPE: PRT

<213> ORGANISM: Cladosporium herbarum

<400> SEQUENCE: 62

Met Lys Tyr Leu Ala Ala Phe Leu Leu Leu Gly Leu Ala Gly Asn Ser
 1 5 10 15

-continued

Ser Pro Ser Ala Glu Asp Ile Lys Thr Val Leu Ser Ser Val Gly Ile
 20 25 30
 Asp Ala Asp Glu Glu Arg Leu Ser Ser Leu Leu Lys Glu Leu Glu Gly
 35 40 45
 Lys Asp Ile Asn Glu Leu Ile Ser Ser Gly Ser Glu Lys Leu Ala Ser
 50 55 60
 Val Pro Ser Gly Gly Ala Gly Ala Ala Ser Ala Gly Gly Ala Ala Ala
 65 70 75 80
 Ala Gly Gly Ala Ala Glu Ala Ala Pro Glu Ala Glu Arg Ala Glu Glu
 85 90 95
 Glu Lys Glu Glu Ser Asp Asp Asp Met Gly Phe Gly Leu Phe Asp Glx
 100 105 110

<210> SEQ ID NO 63
 <211> LENGTH: 204
 <212> TYPE: PRT
 <213> ORGANISM: Cladosporium herbarum

<400> SEQUENCE: 63

Met Ala Pro Lys Ile Ala Ile Ile Phe Tyr Ser Thr Trp Gly His Val
 1 5 10 15
 Gln Thr Leu Ala Glu Ala Glu Ala Lys Gly Ile Arg Glu Ala Gly Gly
 20 25 30
 Ser Val Asp Leu Tyr Arg Val Pro Glu Thr Leu Thr Gln Glu Val Leu
 35 40 45
 Thr Lys Met His Ala Pro Pro Lys Asp Asp Ser Ile Pro Glu Ile Thr
 50 55 60
 Asp Pro Phe Ile Leu Glu Gln Tyr Asp Arg Phe Pro His Gly His Pro
 65 70 75 80
 Thr Arg Tyr Gly Asn Phe Pro Ala Gln Trp Arg Thr Phe Trp Asp Arg
 85 90 95
 Thr Gly Gly Gln Trp Gln Thr Gly Ala Phe Trp Gly Lys Tyr Ala Gly
 100 105 110
 Leu Phe Ile Ser Thr Gly Thr Gln Gly Gly Gly Gln Glu Ser Thr Ala
 115 120 125
 Leu Ala Ala Met Ser Thr Leu Ser His His Gly Ile Ile Tyr Val Pro
 130 135 140
 Leu Gly Tyr Lys Thr Thr Phe His Leu Leu Gly Asp Asn Ser Glu Val
 145 150 155 160
 Arg Gly Ala Ala Val Trp Gly Ala Gly Thr Phe Ser Gly Gly Asp Gly
 165 170 175
 Ser Arg Gln Pro Ser Gln Lys Glu Leu Glu Leu Thr Ala Gln Gly Lys
 180 185 190
 Ala Phe Tyr Glu Ala Val Ala Lys Val Asn Phe Gln
 195 200

<210> SEQ ID NO 64
 <211> LENGTH: 440
 <212> TYPE: PRT
 <213> ORGANISM: Cladosporium herbarum

<400> SEQUENCE: 64

Met Pro Ile Ser Lys Ile His Ser Arg Tyr Val Tyr Asp Ser Arg Gly
 1 5 10 15
 Asn Pro Thr Val Glu Val Asp Ile Val Thr Glu Thr Gly Leu His Arg
 20 25 30

-continued

<210> SEQ ID NO 65
 <211> LENGTH: 110
 <212> TYPE: PRT
 <213> ORGANISM: Cladosporium herbarum

 <400> SEQUENCE: 65

 Met Ser Ala Ala Glu Leu Ala Ser Ser Tyr Ala Ala Leu Ile Leu Ala
 1 5 10 15
 Asp Glu Gly Leu Glu Ile Thr Ala Asp Lys Leu Gln Ala Leu Ile Ser
 20 25 30
 Ala Ala Lys Val Pro Glu Ile Glu Pro Ile Trp Thr Ser Leu Phe Ala
 35 40 45
 Lys Ala Leu Glu Gly Lys Asp Val Lys Asp Leu Leu Leu Asn Val Gly
 50 55 60
 Ser Gly Gly Gly Ala Ala Pro Ala Ala Gly Gly Ala Ala Ala Gly Gly
 65 70 75 80
 Ala Ala Ala Val Leu Asp Ala Pro Ala Glu Glu Lys Ala Glu Glu Glu
 85 90 95
 Lys Glu Glu Ser Asp Asp Asp Met Gly Phe Gly Leu Phe Asp
 100 105 110

<210> SEQ ID NO 66
 <211> LENGTH: 159
 <212> TYPE: PRT
 <213> ORGANISM: Corylus avellana (European hazel)

 <400> SEQUENCE: 66

 Gly Val Phe Asn Tyr Glu Val Glu Thr Pro Ser Val Ile Pro Ala Ala
 1 5 10 15
 Arg Leu Phe Lys Ser Tyr Val Leu Asp Gly Asp Lys Leu Ile Pro Lys
 20 25 30
 Val Ala Pro Gln Ala Ile Thr Ser Val Glu Asn Val Glu Gly Asn Gly
 35 40 45
 Gly Pro Gly Thr Ile Lys Asn Ile Thr Phe Gly Glu Gly Ser Arg Tyr
 50 55 60
 Lys Tyr Val Lys Glu Arg Val Asp Glu Val Asp Asn Thr Asn Phe Thr
 65 70 75 80
 Tyr Ser Tyr Thr Val Ile Glu Gly Asp Val Leu Gly Asp Lys Leu Glu
 85 90 95
 Lys Val Cys His Glu Leu Lys Ile Val Ala Ala Pro Gly Gly Gly Ser
 100 105 110
 Ile Leu Lys Ile Ser Ser Lys Phe His Ala Lys Gly Asp His Glu Ile
 115 120 125
 Asn Ala Glu Glu Met Lys Gly Ala Lys Glu Met Ala Glu Lys Leu Leu
 130 135 140
 Arg Ala Val Glu Thr Tyr Leu Leu Ala His Ser Ala Glu Tyr Asn
 145 150 155

<210> SEQ ID NO 67
 <211> LENGTH: 346
 <212> TYPE: PRT
 <213> ORGANISM: Cupressus arizonica

 <400> SEQUENCE: 67

 Asp Asn Pro Ile Asp Ser Cys Trp Arg Gly Asp Ser Asn Trp Asp Gln
 1 5 10 15
 Asn Arg Met Lys Leu Ala Asp Cys Val Val Gly Phe Gly Ser Ser Thr
 20 25 30

-continued

Met Gly Gly Lys Gly Gly Glu Ile Tyr Thr Val Thr Ser Ser Glu Asp
 35 40 45
 Asn Pro Val Asn Pro Thr Pro Gly Thr Leu Arg Tyr Gly Ala Thr Arg
 50 55 60
 Glu Lys Ala Leu Trp Ile Ile Phe Ser Gln Asn Met Asn Ile Lys Leu
 65 70 75 80
 Gln Met Pro Leu Tyr Val Ala Gly Tyr Lys Thr Ile Asp Gly Arg Gly
 85 90 95
 Ala Val Val His Leu Gly Asn Gly Gly Pro Cys Leu Phe Met Arg Lys
 100 105 110
 Ala Ser His Val Ile Leu His Gly Leu His Ile His Gly Cys Asn Thr
 115 120 125
 Ser Val Leu Gly Asp Val Leu Val Ser Glu Ser Ile Gly Val Glu Pro
 130 135 140
 Val His Ala Gln Asp Gly Asp Ala Ile Thr Met Arg Asn Val Thr Asn
 145 150 155 160
 Ala Trp Ile Asp His Asn Ser Leu Ser Asp Cys Ser Asp Gly Leu Ile
 165 170 175
 Asp Val Thr Leu Gly Ser Thr Gly Ile Thr Ile Ser Asn Asn His Phe
 180 185 190
 Phe Asn His His Lys Val Met Leu Leu Gly His Asp Asp Thr Tyr Asp
 195 200 205
 Asp Asp Lys Ser Met Lys Val Thr Val Ala Phe Asn Gln Phe Gly Pro
 210 215 220
 Asn Ala Gly Gln Arg Met Pro Arg Ala Arg Tyr Gly Leu Val His Val
 225 230 235 240
 Ala Asn Asn Asn Tyr Asp Gln Trp Asn Ile Tyr Ala Ile Gly Gly Ser
 245 250 255
 Ser Asn Pro Thr Ile Leu Ser Glu Gly Asn Ser Phe Thr Ala Pro Asn
 260 265 270
 Glu Ser Tyr Lys Lys Glu Val Thr Lys Arg Ile Gly Cys Glu Thr Thr
 275 280 285
 Ser Ala Cys Ala Asn Trp Val Trp Arg Ser Thr Arg Asp Ala Phe Thr
 290 295 300
 Asn Gly Ala Tyr Phe Val Ser Ser Gly Lys Ala Glu Asp Thr Asn Ile
 305 310 315 320
 Tyr Asn Ser Asn Glu Ala Phe Lys Val Glu Asn Gly Asn Ala Ala Pro
 325 330 335
 Gln Leu Thr Gln Asn Ala Gly Val Val Ala
 340 345

<210> SEQ ID NO 68

<211> LENGTH: 374

<212> TYPE: PRT

<213> ORGANISM: Cryptomeria japonica (Japanese cedar)

<400> SEQUENCE: 68

Met Asp Ser Pro Cys Leu Val Ala Leu Leu Val Leu Ser Phe Val Ile
 1 5 10 15
 Gly Ser Cys Phe Ser Asp Asn Pro Ile Asp Ser Cys Trp Arg Gly Asp
 20 25 30
 Ser Asn Trp Ala Gln Asn Arg Met Lys Leu Ala Asp Cys Ala Val Gly
 35 40 45
 Phe Gly Ser Ser Thr Met Gly Gly Lys Gly Gly Asp Leu Tyr Thr Val

-continued

50	55	60
Thr Asn Ser Asp Asp Asp Pro Val Asn Pro Ala Pro Gly Thr Leu Arg 65 70 75 80		
Tyr Gly Ala Thr Arg Asp Arg Pro Leu Trp Ile Ile Phe Ser Gly Asn 85 90 95		
Met Asn Ile Lys Leu Lys Met Pro Met Tyr Ile Ala Gly Tyr Lys Thr 100 105 110		
Phe Asp Gly Arg Gly Ala Gln Val Tyr Ile Gly Asn Gly Gly Pro Cys 115 120 125		
Val Phe Ile Lys Arg Val Ser Asn Val Ile Ile His Gly Leu His Leu 130 135 140		
Tyr Gly Cys Ser Thr Ser Val Leu Gly Asn Val Leu Ile Asn Glu Ser 145 150 155 160		
Phe Gly Val Glu Pro Val His Pro Gln Asp Gly Asp Ala Leu Thr Leu 165 170 175		
Arg Thr Ala Thr Asn Ile Trp Ile Asp His Asn Ser Phe Ser Asn Ser 180 185 190		
Ser Asp Gly Leu Val Asp Val Thr Leu Ser Ser Thr Gly Val Thr Ile 195 200 205		
Ser Asn Asn Leu Phe Phe Asn His His Lys Val Met Leu Leu Gly His 210 215 220		
Asp Asp Ala Tyr Ser Asp Asp Lys Ser Met Lys Val Thr Val Ala Phe 225 230 235 240		
Asn Gln Phe Gly Pro Asn Cys Gly Gln Arg Met Pro Arg Ala Arg Tyr 245 250 255		
Gly Leu Val His Val Ala Asn Asn Asn Tyr Asp Pro Trp Thr Ile Tyr 260 265 270		
Ala Ile Gly Gly Ser Ser Asn Pro Thr Ile Leu Ser Glu Gly Asn Ser 275 280 285		
Phe Thr Ala Pro Asn Glu Ser Tyr Lys Lys Gln Val Thr Ile Arg Ile 290 295 300		
Gly Cys Lys Thr Ser Ser Ser Cys Ser Asn Trp Val Trp Gln Ser Thr 305 310 315 320		
Gln Asp Val Phe Tyr Asn Gly Ala Tyr Phe Val Ser Ser Gly Lys Tyr 325 330 335		
Glu Gly Gly Asn Ile Tyr Thr Lys Lys Glu Ala Phe Asn Val Glu Asn 340 345 350		
Gly Asn Ala Thr Pro Gln Leu Thr Lys Asn Ala Gly Val Leu Thr Cys 355 360 365		
Ser Leu Ser Lys Arg Cys 370		

<210> SEQ ID NO 69

<211> LENGTH: 514

<212> TYPE: PRT

<213> ORGANISM: Cryptomeria japonica (Japanese cedar)

<400> SEQUENCE: 69

Met Ala Met Lys Phe Ile Ala Pro Met Ala Phe Val Ala Met Gln Leu 1 5 10 15
Ile Ile Met Ala Ala Ala Glu Asp Gln Ser Ala Gln Ile Met Leu Asp 20 25 30
Ser Asp Ile Glu Gln Tyr Leu Arg Ser Asn Arg Ser Leu Arg Lys Val 35 40 45

-continued

Glu	His	Ser	Arg	His	Asp	Ala	Ile	Asn	Ile	Phe	Asn	Val	Glu	Lys	Tyr
50						55					60				
Gly	Ala	Val	Gly	Asp	Gly	Lys	His	Asp	Cys	Thr	Glu	Ala	Phe	Ser	Thr
65					70					75					80
Ala	Trp	Gln	Ala	Ala	Cys	Lys	Lys	Pro	Ser	Ala	Met	Leu	Leu	Val	Pro
				85					90					95	
Gly	Asn	Lys	Lys	Phe	Val	Val	Asn	Asn	Leu	Phe	Phe	Asn	Gly	Pro	Cys
			100					105					110		
Gln	Pro	His	Phe	Thr	Phe	Lys	Val	Asp	Gly	Ile	Ile	Ala	Ala	Tyr	Gln
		115						120					125		
Asn	Pro	Ala	Ser	Trp	Lys	Asn	Asn	Arg	Ile	Trp	Leu	Gln	Phe	Ala	Lys
		130					135				140				
Leu	Thr	Gly	Phe	Thr	Leu	Met	Gly	Lys	Gly	Val	Ile	Asp	Gly	Gln	Gly
145					150					155					160
Lys	Gln	Trp	Trp	Ala	Gly	Gln	Cys	Lys	Trp	Val	Asn	Gly	Arg	Glu	Ile
				165						170				175	
Cys	Asn	Asp	Arg	Asp	Arg	Pro	Thr	Ala	Ile	Lys	Phe	Asp	Phe	Ser	Thr
			180						185				190		
Gly	Leu	Ile	Ile	Gln	Gly	Leu	Lys	Leu	Met	Asn	Ser	Pro	Glu	Phe	His
		195						200				205			
Leu	Val	Phe	Gly	Asn	Cys	Glu	Gly	Val	Lys	Ile	Ile	Gly	Ile	Ser	Ile
	210						215					220			
Thr	Ala	Pro	Arg	Asp	Ser	Pro	Asn	Thr	Asp	Gly	Ile	Asp	Ile	Phe	Ala
225						230				235					240
Ser	Lys	Asn	Phe	His	Leu	Gln	Lys	Asn	Thr	Ile	Gly	Thr	Gly	Asp	Asp
				245					250					255	
Cys	Val	Ala	Ile	Gly	Thr	Gly	Ser	Ser	Asn	Ile	Val	Ile	Glu	Asp	Leu
			260						265				270		
Ile	Cys	Gly	Pro	Gly	His	Gly	Ile	Ser	Ile	Gly	Ser	Leu	Gly	Arg	Glu
		275					280					285			
Asn	Ser	Arg	Ala	Glu	Val	Ser	Tyr	Val	His	Val	Asn	Gly	Ala	Lys	Phe
						295					300				
Ile	Asp	Thr	Gln	Asn	Gly	Leu	Arg	Ile	Lys	Thr	Trp	Gln	Gly	Gly	Ser
305					310					315					320
Gly	Met	Ala	Ser	His	Ile	Ile	Tyr	Glu	Asn	Val	Glu	Met	Ile	Asn	Ser
				325					330					335	
Glu	Asn	Pro	Ile	Leu	Ile	Asn	Gln	Phe	Tyr	Cys	Thr	Ser	Ala	Ser	Ala
			340					345						350	
Cys	Gln	Asn	Gln	Arg	Ser	Ala	Val	Gln	Ile	Gln	Asp	Val	Thr	Tyr	Lys
		355						360				365			
Asn	Ile	Arg	Gly	Thr	Ser	Ala	Thr	Ala	Ala	Ala	Ile	Gln	Leu	Lys	Cys
						375						380			
Ser	Asp	Ser	Met	Pro	Cys	Lys	Asp	Ile	Lys	Leu	Ser	Asp	Ile	Ser	Leu
385					390					395					400
Lys	Leu	Thr	Ser	Gly	Lys	Ile	Ala	Ser	Cys	Leu	Asn	Asp	Asn	Ala	Asn
				405					410					415	
Gly	Tyr	Phe	Ser	Gly	His	Val	Ile	Pro	Ala	Cys	Lys	Asn	Leu	Ser	Pro
			420					425					430		
Ser	Ala	Lys	Arg	Lys	Glu	Ser	Lys	Ser	His	Lys	His	Pro	Lys	Thr	Val
		435					440					445			
Met	Val	Lys	Asn	Met	Gly	Ala	Tyr	Asp	Lys	Gly	Asn	Arg	Thr	Arg	Ile
	450					455					460				
Leu	Leu	Gly	Ser	Arg	Pro	Pro	Asn	Cys	Thr	Asn	Lys	Cys	His	Gly	Cys

-continued

Gly Ala Gly Thr Val Arg Ile Ile Thr Leu Pro Glu Gly Ser Pro Ile
 50 55 60
 Thr Ser Met Thr Val Arg Thr Asp Ala Val Asn Lys Glu Ala Leu Thr
 65 70 75 80
 Tyr Asp Ser Thr Val Ile Asp Gly Asp Ile Leu Leu Gly Phe Ile Glu
 85 90 95
 Ser Ile Glu Thr His Leu Val Val Val Pro Thr Ala Asp Gly Gly Ser
 100 105 110
 Ile Thr Lys Thr Thr Ala Ile Phe His Thr Lys Gly Asp Ala Val Val
 115 120 125
 Pro Glu Glu Asn Ile Lys Phe Ala Asp Ala Gln Asn Thr Ala Leu Phe
 130 135 140
 Lys Ala Ile Glu Ala Tyr Leu Ile Ala Asn
 145 150

<210> SEQ ID NO 73

<211> LENGTH: 321

<212> TYPE: PRT

<213> ORGANISM: Dermatophagoides farinae (House-dust mite)

<400> SEQUENCE: 73

Met Lys Phe Val Leu Ala Ile Ala Ser Leu Leu Val Leu Ser Thr Val
 1 5 10 15
 Tyr Ala Arg Pro Ala Ser Ile Lys Thr Phe Glu Glu Phe Lys Lys Ala
 20 25 30
 Phe Asn Lys Asn Tyr Ala Thr Val Glu Glu Glu Val Ala Arg Lys
 35 40 45
 Asn Phe Leu Glu Ser Leu Lys Tyr Val Glu Ala Asn Lys Gly Ala Ile
 50 55 60
 Asn His Leu Ser Asp Leu Ser Leu Asp Glu Phe Lys Asn Arg Tyr Leu
 65 70 75 80
 Met Ser Ala Glu Ala Phe Glu Gln Leu Lys Thr Gln Phe Asp Leu Asn
 85 90 95
 Ala Glu Thr Ser Ala Cys Arg Ile Asn Ser Val Asn Val Pro Ser Glu
 100 105 110
 Leu Asp Leu Arg Ser Leu Arg Thr Val Thr Pro Ile Arg Met Gln Gly
 115 120 125
 Gly Cys Gly Ser Cys Trp Ala Phe Ser Gly Val Ala Ala Thr Glu Ser
 130 135 140
 Ala Tyr Leu Ala Tyr Arg Asn Thr Ser Leu Asp Leu Ser Glu Gln Glu
 145 150 155 160
 Leu Val Asp Cys Ala Ser Gln His Gly Cys His Gly Asp Thr Ile Pro
 165 170 175
 Arg Gly Ile Glu Tyr Ile Gln Gln Asn Gly Val Val Glu Glu Arg Ser
 180 185 190
 Tyr Pro Tyr Val Ala Arg Glu Gln Arg Cys Arg Arg Pro Asn Ser Gln
 195 200 205
 His Tyr Gly Ile Ser Asn Tyr Cys Gln Ile Tyr Pro Pro Asp Val Lys
 210 215 220
 Gln Ile Arg Glu Ala Leu Thr Gln Thr His Thr Ala Ile Ala Val Ile
 225 230 235 240
 Ile Gly Ile Lys Asp Leu Arg Ala Phe Gln His Tyr Asp Gly Arg Thr
 245 250 255
 Ile Ile Gln His Asp Asn Gly Tyr Gln Pro Asn Tyr His Ala Val Asn
 260 265 270

-continued

Ile Val Gly Tyr Gly Ser Thr Gln Gly Asp Asp Tyr Trp Ile Val Arg
 275 280 285
 Asn Ser Trp Asp Thr Thr Trp Gly Asp Ser Gly Tyr Gly Tyr Phe Gln
 290 295 300
 Ala Gly Asn Asn Leu Met Met Ile Glu Gln Tyr Pro Tyr Val Val Ile
 305 310 315 320
 Met

<210> SEQ ID NO 74
 <211> LENGTH: 146
 <212> TYPE: PRT
 <213> ORGANISM: Dermatophagoides farinae (House-dust mite)

<400> SEQUENCE: 74

Met Ile Ser Lys Ile Leu Cys Leu Ser Leu Leu Val Ala Ala Val Val
 1 5 10 15
 Ala Asp Gln Val Asp Val Lys Asp Cys Ala Asn Asn Glu Ile Lys Lys
 20 25 30
 Val Met Val Asp Gly Cys His Gly Ser Asp Pro Cys Ile Ile His Arg
 35 40 45
 Gly Lys Pro Phe Thr Leu Glu Ala Leu Phe Asp Ala Asn Gln Asn Thr
 50 55 60
 Lys Thr Ala Lys Ile Glu Ile Lys Ala Ser Leu Asp Gly Leu Glu Ile
 65 70 75 80
 Asp Val Pro Gly Ile Asp Thr Asn Ala Cys His Phe Met Lys Cys Pro
 85 90 95
 Leu Val Lys Gly Gln Gln Tyr Asp Ile Lys Tyr Thr Trp Asn Val Pro
 100 105 110
 Lys Ile Ala Pro Lys Ser Glu Asn Val Val Val Thr Val Lys Leu Ile
 115 120 125
 Gly Asp Asn Gly Val Leu Ala Cys Ala Ile Ala Thr His Gly Lys Ile
 130 135 140
 Arg Asp
 145

<210> SEQ ID NO 75
 <211> LENGTH: 259
 <212> TYPE: PRT
 <213> ORGANISM: Dermatophagoides farinae (House-dust mite)

<400> SEQUENCE: 75

Met Met Ile Leu Thr Ile Val Val Leu Leu Ala Ala Asn Ile Leu Ala
 1 5 10 15
 Thr Pro Ile Leu Pro Ser Ser Pro Asn Ala Thr Ile Val Gly Gly Val
 20 25 30
 Lys Ala Gln Ala Gly Asp Cys Pro Tyr Gln Ile Ser Leu Gln Ser Ser
 35 40 45
 Ser His Phe Cys Gly Gly Ser Ile Leu Asp Glu Tyr Trp Ile Leu Thr
 50 55 60
 Ala Ala His Cys Val Asn Gly Gln Ser Ala Lys Lys Leu Ser Ile Arg
 65 70 75 80
 Tyr Asn Thr Leu Lys His Ala Ser Gly Gly Glu Lys Ile Gln Val Ala
 85 90 95
 Glu Ile Tyr Gln His Glu Asn Tyr Asp Ser Met Thr Ile Asp Asn Asp
 100 105 110

-continued

225	230	235	240
Gly Ile Lys Asp	Leu Asp Ala Phe Arg His Tyr Asp Gly Arg Thr Ile		
	245	250	255
Ile Gln Arg Asp	Asn Gly Tyr Gln Pro Asn Tyr His Ala Val Asn Ile		
	260	265	270
Val Gly Tyr Ser	Asn Ala Gln Gly Val Asp Tyr Trp Ile Val Arg Asn		
	275	280	285
Ser Trp Asp Thr	Asn Trp Gly Asp Asn Gly Tyr Gly Tyr Phe Ala Ala		
	290	295	300
Asn Ile Asp Leu Met	Met Ile Glu Glu Tyr Pro Tyr Val Val Ile Leu		
305	310	315	320

<210> SEQ ID NO 80
 <211> LENGTH: 146
 <212> TYPE: PRT
 <213> ORGANISM: Dermatophagoides pteronyssinus (House-dust mite)

<400> SEQUENCE: 80

Met Met Tyr Lys	Ile Leu Cys Leu Ser Leu Leu Val Ala Ala Val Ala		
1	5	10	15
Arg Asp Gln Val	Asp Val Lys Asp Cys Ala Asn His Glu Ile Lys Lys		
	20	25	30
Val Leu Val Pro	Gly Cys His Gly Ser Glu Pro Cys Ile Ile His Arg		
	35	40	45
Gly Lys Pro Phe	Gln Leu Glu Ala Val Phe Glu Ala Asn Gln Asn Thr		
	50	55	60
Lys Thr Ala Lys	Ile Glu Ile Lys Ala Ser Ile Asp Gly Leu Glu Val		
65	70	75	80
Asp Val Pro Gly	Ile Asp Pro Asn Ala Cys His Tyr Met Lys Cys Pro		
	85	90	95
Leu Val Lys Gly	Gln Gln Tyr Asp Ile Lys Tyr Thr Trp Asn Val Pro		
	100	105	110
Lys Ile Ala Pro	Lys Ser Glu Asn Val Val Val Thr Val Lys Val Met		
	115	120	125
Gly Asp Asp Gly	Val Leu Ala Cys Ala Ile Ala Thr His Ala Lys Ile		
	130	135	140
Arg Asp			
145			

<210> SEQ ID NO 81
 <211> LENGTH: 261
 <212> TYPE: PRT
 <213> ORGANISM: Dermatophagoides pteronyssinus (House-dust mite)

<400> SEQUENCE: 81

Met Ile Ile Tyr	Asn Ile Leu Ile Val Leu Leu Leu Ala Ile Asn Thr		
1	5	10	15
Leu Ala Asn Pro	Ile Leu Pro Ala Ser Pro Asn Ala Thr Ile Val Gly		
	20	25	30
Gly Glu Lys Ala	Leu Ala Gly Glu Cys Pro Tyr Gln Ile Ser Leu Gln		
	35	40	45
Ser Ser Ser His	Phe Cys Gly Gly Thr Ile Leu Asp Glu Tyr Trp Ile		
	50	55	60
Leu Thr Ala Ala	His Cys Val Ala Gly Gln Thr Ala Ser Lys Leu Ser		
65	70	75	80
Ile Arg Tyr Asn	Ser Leu Lys His Ser Leu Gly Gly Glu Lys Ile Ser		

-continued

	85		90		95										
Val	Ala	Lys	Ile	Phe	Ala	His	Glu	Lys	Tyr	Asp	Ser	Tyr	Gln	Ile	Asp
			100					105					110		
Asn	Asp	Ile	Ala	Leu	Ile	Lys	Leu	Lys	Ser	Pro	Met	Lys	Leu	Asn	Gln
		115					120					125			
Lys	Asn	Ala	Lys	Ala	Val	Gly	Leu	Pro	Ala	Lys	Gly	Ser	Asp	Val	Lys
	130					135					140				
Val	Gly	Asp	Gln	Val	Arg	Val	Ser	Gly	Trp	Gly	Tyr	Leu	Glu	Glu	Gly
145					150					155					160
Ser	Tyr	Ser	Leu	Pro	Ser	Glu	Leu	Arg	Arg	Val	Asp	Ile	Ala	Val	Val
				165					170					175	
Ser	Arg	Lys	Glu	Cys	Asn	Glu	Leu	Tyr	Ser	Lys	Ala	Asn	Ala	Glu	Val
			180					185					190		
Thr	Asp	Asn	Met	Ile	Cys	Gly	Gly	Asp	Val	Ala	Asn	Gly	Gly	Lys	Asp
		195					200					205			
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Val	Val	Asp	Val	Lys	Asn	Asn
	210					215					220				
Gln	Val	Val	Gly	Ile	Val	Ser	Trp	Gly	Tyr	Gly	Cys	Ala	Arg	Lys	Gly
225					230					235					240
Tyr	Pro	Gly	Val	Tyr	Thr	Arg	Val	Gly	Asn	Phe	Ile	Asp	Trp	Ile	Glu
				245					250					255	
Ser	Lys	Arg	Ser	Gln											
				260											

<210> SEQ ID NO 82
 <211> LENGTH: 19
 <212> TYPE: PRT
 <213> ORGANISM: Dermatophagoides pteronyssinus (House-dust mite)
 <220> FEATURE:
 <221> NAME/KEY: UNSURE
 <222> LOCATION: 3, 16
 <223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 82

Lys	Tyr	Xaa	Asn	Pro	His	Phe	Ile	Gly	Xaa	Arg	Ser	Val	Ile	Thr	Xaa
1			5					10					15		

Leu Met Glu

<210> SEQ ID NO 83
 <211> LENGTH: 132
 <212> TYPE: PRT
 <213> ORGANISM: Dermatophagoides pteronyssinus (House-dust mite)

<400> SEQUENCE: 83

Met	Lys	Phe	Ile	Ile	Ala	Phe	Phe	Val	Ala	Thr	Leu	Ala	Val	Met	Thr
1				5					10					15	

Val	Ser	Gly	Glu	Asp	Lys	Lys	His	Asp	Tyr	Gln	Asn	Glu	Phe	Asp	Phe
			20					25					30		

Leu	Leu	Met	Glu	Arg	Ile	His	Glu	Gln	Ile	Lys	Lys	Gly	Glu	Leu	Ala
		35					40					45			

Leu	Phe	Tyr	Leu	Gln	Glu	Gln	Ile	Asn	His	Phe	Glu	Glu	Lys	Pro	Thr
	50					55					60				

Lys	Glu	Met	Lys	Asp	Lys	Ile	Val	Ala	Glu	Met	Asp	Thr	Ile	Ile	Ala
65					70					75					80

Met	Ile	Asp	Gly	Val	Arg	Gly	Val	Leu	Asp	Arg	Leu	Met	Gln	Arg	Lys
				85					90				95		

Asp Leu Asp Ile Phe Glu Gln Tyr Asn Leu Glu Met Ala Lys Lys Ser

-continued

100	105	110
Gly Asp Ile Leu Glu Arg Asp Leu Lys Lys Glu Glu Ala Arg Val Lys		
115	120	125
Lys Ile Glu Val		
130		

<210> SEQ ID NO 84
 <211> LENGTH: 20
 <212> TYPE: PRT
 <213> ORGANISM: Dermatophagoides pteronyssinus (House-dust mite)
 <220> FEATURE:
 <221> NAME/KEY: UNSURE
 <222> LOCATION: 4
 <223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 84

Ala Ile Gly Xaa Gln Pro Ala Ala Glu Ala Glu Ala Pro Phe Gln Ile		
1	5	10
		15

Ser Leu Met Lys		
20		

<210> SEQ ID NO 85
 <211> LENGTH: 215
 <212> TYPE: PRT
 <213> ORGANISM: Dermatophagoides pteronyssinus (House-dust mite)

<400> SEQUENCE: 85

Met Met Lys Leu Leu Leu Ile Ala Ala Ala Ala Phe Val Ala Val Ser		
1	5	10
		15

Ala Asp Pro Ile His Tyr Asp Lys Ile Thr Glu Glu Ile Asn Lys Ala		
20	25	30

Val Asp Glu Ala Val Ala Ala Ile Glu Lys Ser Glu Thr Phe Asp Pro		
35	40	45

Met Lys Val Pro Asp His Ser Asp Lys Phe Glu Arg His Ile Gly Ile		
50	55	60

Ile Asp Leu Lys Gly Glu Leu Asp Met Arg Asn Ile Gln Val Arg Gly		
65	70	75
		80

Leu Lys Gln Met Lys Arg Val Gly Asp Ala Asn Val Lys Ser Glu Asp		
85	90	95

Gly Val Val Lys Ala His Leu Leu Val Gly Val His Asp Asp Val Val		
100	105	110

Ser Met Glu Tyr Asp Leu Ala Tyr Lys Leu Gly Asp Leu His Pro Asn		
115	120	125

Thr His Val Ile Ser Asp Ile Gln Asp Phe Val Val Glu Leu Ser Leu		
130	135	140

Glu Val Ser Glu Glu Gly Asn Met Thr Leu Thr Ser Phe Glu Val Arg		
145	150	155
		160

Gln Phe Ala Asn Val Val Asn His Ile Gly Gly Leu Ser Ile Leu Asp		
165	170	175

Pro Ile Phe Ala Val Leu Ser Asp Val Leu Thr Ala Ile Phe Gln Asp		
180	185	190

Thr Val Arg Ala Glu Met Thr Lys Val Leu Ala Pro Ala Phe Lys Lys		
195	200	205

Glu Leu Glu Arg Asn Asn Gln		
210	215	

<210> SEQ ID NO 86
 <211> LENGTH: 203

-continued

<212> TYPE: PRT

<213> ORGANISM: Dolichovespula arenaria (Yellow hornet)

<400> SEQUENCE: 86

Asn Asn Tyr Cys Lys Ile Cys Pro Lys Gly Thr His Thr Leu Cys Lys
 1 5 10 15
 Tyr Gly Thr Ser Met Lys Pro Asn Cys Gly Gly Lys Ile Val Lys Ser
 20 25 30
 Tyr Gly Val Thr Asn Asp Glu Lys Asn Glu Ile Val Lys Arg His Asn
 35 40 45
 Glu Phe Arg Gln Lys Val Ala Gln Gly Leu Glu Thr Arg Gly Asn Pro
 50 55 60
 Gly Pro Gln Pro Pro Ala Lys Asn Met Asn Leu Leu Val Trp Asn Asp
 65 70 75 80
 Glu Leu Ala Lys Ile Ala Gln Thr Trp Ala Asn Gln Cys Asn Phe Gly
 85 90 95
 His Asp Gln Cys Arg Asn Thr Ala Lys Tyr Pro Val Gly Gln Asn Val
 100 105 110
 Ala Ile Ala Ser Thr Thr Gly Asn Ser Tyr Gln Thr Met Ser Tyr Leu
 115 120 125
 Ile Lys Met Trp Glu Asp Glu Val Lys Asp Tyr Asn Pro His Lys Asp
 130 135 140
 Leu Met His Asn Asn Phe Ser Lys Val Gly His Tyr Thr Gln Met Val
 145 150 155 160
 Trp Gly Lys Thr Lys Glu Ile Gly Cys Gly Ser Val Lys Tyr Ile Glu
 165 170 175
 Asn Lys Trp His Thr His Tyr Leu Val Cys Asn Tyr Gly Pro Ala Gly
 180 185 190
 Asn Tyr Met Asn Gln Pro Val Tyr Glu Arg Lys
 195 200

<210> SEQ ID NO 87

<211> LENGTH: 317

<212> TYPE: PRT

<213> ORGANISM: Dolichovespula maculata (White-face hornet)

<400> SEQUENCE: 87

Arg Leu Ile Met Phe Val Gly Asp Pro Ser Ser Ser Asn Glu Leu Asp
 1 5 10 15
 Arg Phe Ser Val Cys Pro Phe Ser Asn Asp Thr Val Lys Met Ile Phe
 20 25 30
 Leu Thr Arg Glu Asn Arg Lys His Asp Phe Tyr Thr Leu Asp Thr Met
 35 40 45
 Asn Arg His Asn Glu Phe Lys Lys Ser Ile Ile Lys Arg Pro Val Val
 50 55 60
 Phe Ile Thr His Gly Phe Thr Ser Ser Ala Thr Glu Lys Asn Phe Val
 65 70 75 80
 Ala Met Ser Glu Ala Leu Met His Thr Gly Asp Phe Leu Ile Ile Met
 85 90 95
 Val Asp Trp Arg Met Ala Ala Cys Thr Asp Glu Tyr Pro Gly Leu Lys
 100 105 110
 Tyr Met Phe Tyr Lys Ala Ala Val Gly Asn Thr Arg Leu Val Gly Asn
 115 120 125
 Phe Ile Ala Met Ile Ala Lys Lys Leu Val Glu Gln Tyr Lys Val Pro
 130 135 140

-continued

Met Thr Asn Ile Arg Leu Val Gly His Ser Leu Gly Ala His Ile Ser
145 150 155 160

Gly Phe Ala Gly Lys Arg Val Gln Glu Leu Lys Leu Gly Lys Phe Ser
165 170 175

Glu Ile Ile Gly Leu Asp Pro Ala Gly Pro Ser Phe Lys Lys Asn Asp
180 185 190

Cys Ser Glu Arg Ile Cys Glu Thr Asp Ala His Tyr Val Gln Ile Leu
195 200 205

His Thr Ser Ser Asn Leu Gly Thr Glu Arg Thr Leu Gly Thr Val Asp
210 215 220

Phe Tyr Ile Asn Asn Gly Ser Asn Gln Pro Gly Cys Arg Tyr Ile Ile
225 230 235 240

Gly Glu Thr Cys Ser His Thr Arg Ala Val Lys Tyr Phe Thr Glu Cys
245 250 255

Ile Arg Arg Glu Cys Cys Leu Ile Gly Val Pro Gln Ser Lys Asn Pro
260 265 270

Gln Pro Val Ser Lys Cys Thr Arg Asn Glu Cys Val Cys Val Gly Leu
275 280 285

Asn Ala Lys Lys Tyr Pro Lys Arg Gly Ser Phe Tyr Val Pro Val Glu
290 295 300

Ala Glu Ala Pro Tyr Cys Asn Asn Asn Gly Lys Ile Ile
305 310 315

<210> SEQ ID NO 88

<211> LENGTH: 303

<212> TYPE: PRT

<213> ORGANISM: Dolichovespula maculata (White-face hornet)

<400> SEQUENCE: 88

Gly Ile Leu Pro Glu Cys Lys Leu Val Pro Glu Glu Ile Ser Phe Val
1 5 10 15

Leu Ser Thr Arg Glu Asn Arg Asp Gly Val Tyr Leu Thr Leu Gln Lys
20 25 30

Leu Lys Asn Gly Lys Met Phe Lys Asn Ser Asp Leu Ser Ser Lys Lys
35 40 45

Val Pro Phe Leu Ile His Gly Phe Ile Ser Ser Ala Thr Asn Lys Asn
50 55 60

Tyr Ala Asp Met Thr Arg Ala Leu Leu Asp Lys Asp Asp Ile Met Val
65 70 75 80

Ile Ser Ile Asp Trp Arg Asp Gly Ala Cys Ser Asn Glu Phe Ala Leu
85 90 95

Leu Lys Phe Ile Gly Tyr Pro Lys Ala Val Glu Asn Thr Arg Ala Val
100 105 110

Gly Lys Tyr Ile Ala Asp Phe Ser Lys Ile Leu Ile Gln Lys Tyr Lys
115 120 125

Val Leu Leu Glu Asn Ile Arg Leu Ile Gly His Ser Leu Gly Ala Gln
130 135 140

Ile Ala Gly Phe Ala Gly Lys Glu Phe Gln Arg Phe Lys Leu Gly Lys
145 150 155 160

Tyr Pro Glu Ile Ile Gly Leu Asp Pro Ala Gly Pro Ser Phe Lys Lys
165 170 175

Lys Asp Cys Pro Glu Arg Ile Cys Glu Thr Asp Ala His Tyr Val Gln
180 185 190

Ile Leu His Thr Ser Ser Asn Leu Gly Thr Glu Arg Thr Leu Gly Thr
195 200 205

-continued

Val Asp Phe Tyr Ile Asn Asp Gly Ser Asn Gln Pro Gly Cys Thr Tyr
 210 215 220

Ile Ile Gly Glu Thr Cys Ser His Thr Arg Ala Val Lys Tyr Leu Thr
 225 230 235 240

Glu Cys Ile Arg Arg Glu Cys Cys Leu Ile Gly Val Pro Gln Ser Lys
 245 250 255

Asn Pro Gln Pro Val Ser Lys Cys Thr Arg Asn Glu Cys Val Cys Val
 260 265 270

Gly Leu Asn Ala Lys Glu Tyr Pro Lys Lys Gly Ser Phe Tyr Val Pro
 275 280 285

Val Glu Ala Lys Ala Pro Phe Cys Asn Asn Asn Gly Lys Ile Ile
 290 295 300

<210> SEQ ID NO 89
 <211> LENGTH: 331
 <212> TYPE: PRT
 <213> ORGANISM: Dolichovespula maculata (White-face hornet)

<400> SEQUENCE: 89

Ser Glu Arg Pro Lys Arg Val Phe Asn Ile Tyr Trp Asn Val Pro Thr
 1 5 10 15

Phe Met Cys His Gln Tyr Gly Leu Tyr Phe Asp Glu Val Thr Asn Phe
 20 25 30

Asn Ile Lys His Asn Ser Lys Asp Asp Phe Gln Gly Asp Lys Ile Ser
 35 40 45

Ile Phe Tyr Asp Pro Gly Glu Phe Pro Ala Leu Leu Pro Leu Lys Glu
 50 55 60

Gly Asn Tyr Lys Ile Arg Asn Gly Gly Val Pro Gln Glu Gly Asn Ile
 65 70 75 80

Thr Ile His Leu Gln Arg Phe Ile Glu Asn Leu Asp Lys Thr Tyr Pro
 85 90 95

Asn Arg Asn Phe Asn Gly Ile Gly Val Ile Asp Phe Glu Arg Trp Arg
 100 105 110

Pro Ile Phe Arg Gln Asn Trp Gly Asn Met Met Ile His Lys Lys Phe
 115 120 125

Ser Ile Asp Leu Val Arg Asn Glu His Pro Phe Trp Asp Lys Lys Met
 130 135 140

Ile Glu Leu Glu Ala Ser Lys Arg Phe Glu Lys Tyr Ala Arg Leu Phe
 145 150 155 160

Met Glu Glu Thr Leu Lys Leu Ala Lys Lys Thr Arg Lys Gln Ala Asp
 165 170 175

Trp Gly Tyr Tyr Gly Tyr Pro Tyr Cys Phe Asn Met Ser Pro Asn Asn
 180 185 190

Leu Val Pro Asp Cys Asp Ala Thr Ala Met Leu Glu Asn Asp Lys Met
 195 200 205

Ser Trp Leu Phe Asn Asn Gln Asn Val Leu Leu Pro Ser Val Tyr Ile
 210 215 220

Arg His Glu Leu Thr Pro Asp Gln Arg Val Gly Leu Val Gln Gly Arg
 225 230 235 240

Val Lys Glu Ala Val Arg Ile Ser Asn Asn Leu Lys His Ser Pro Lys
 245 250 255

Val Leu Ser Tyr Trp Trp Tyr Val Tyr Gln Asp Asp Thr Asn Thr Phe
 260 265 270

Leu Thr Glu Thr Asp Val Lys Lys Thr Phe Gln Glu Ile Ala Ile Asn

-continued

275	280	285																	
Gly	Gly	Asp	Gly	Ile	Ile	Ile	Trp	Gly	Ser	Ser	Ser	Asp	Val	Asn	Ser				
290						295					300								
Leu	Ser	Lys	Cys	Lys	Arg	Leu	Arg	Glu	Tyr	Leu	Leu	Thr	Val	Leu	Gly				
305					310					315					320				
Pro	Ile	Thr	Val	Asn	Val	Thr	Glu	Thr	Val	Asn									
				325						330									

<210> SEQ ID NO 90
 <211> LENGTH: 227
 <212> TYPE: PRT
 <213> ORGANISM: Dolichovespula maculata (White-face hornet)

<400> SEQUENCE: 90

Met	Glu	Ile	Gly	Gly	Leu	Val	Tyr	Leu	Ile	Leu	Ile	Ile	Thr	Ile	Ile				
1				5				10						15					
Asn	Leu	Ser	Phe	Gly	Glu	Thr	Asn	Asn	Tyr	Cys	Lys	Ile	Lys	Cys	Arg				
			20					25					30						
Lys	Gly	Ile	His	Thr	Leu	Cys	Lys	Phe	Gly	Thr	Ser	Met	Lys	Pro	Asn				
		35					40					45							
Cys	Gly	Arg	Asn	Val	Val	Lys	Ala	Tyr	Gly	Leu	Thr	Asn	Asp	Glu	Lys				
50						55					60								
Asn	Glu	Ile	Leu	Lys	Arg	His	Asn	Asp	Phe	Arg	Gln	Asn	Val	Ala	Lys				
65					70					75					80				
Gly	Leu	Glu	Thr	Arg	Gly	Lys	Pro	Gly	Pro	Gln	Pro	Pro	Ala	Lys	Asn				
				85				90						95					
Met	Asn	Val	Leu	Val	Trp	Asn	Asp	Glu	Leu	Ala	Lys	Ile	Ala	Gln	Thr				
			100					105					110						
Trp	Ala	Asn	Gln	Cys	Asp	Phe	Asn	His	Asp	Asp	Cys	Arg	Asn	Thr	Ala				
	115						120					125							
Lys	Tyr	Gln	Val	Gly	Gln	Asn	Ile	Ala	Ile	Ser	Ser	Thr	Thr	Ala	Thr				
	130					135						140							
Gln	Phe	Asp	Arg	Pro	Ser	Lys	Leu	Ile	Lys	Gln	Trp	Glu	Asp	Glu	Val				
145					150					155					160				
Thr	Glu	Phe	Asn	Tyr	Lys	Val	Gly	Leu	Gln	Asn	Ser	Asn	Phe	Arg	Lys				
			165					170						175					
Val	Gly	His	Tyr	Thr	Gln	Met	Val	Trp	Gly	Lys	Thr	Lys	Glu	Ile	Gly				
			180					185					190						
Cys	Gly	Ser	Ile	Lys	Tyr	Ile	Glu	Asp	Asn	Trp	Tyr	Thr	His	Tyr	Leu				
	195						200					205							
Val	Cys	Asn	Tyr	Gly	Pro	Gly	Gly	Asn	Asp	Phe	Asn	Gln	Pro	Ile	Tyr				
	210					215					220								
Glu	Arg	Lys																	
225																			

<210> SEQ ID NO 91
 <211> LENGTH: 215
 <212> TYPE: PRT
 <213> ORGANISM: Dolichovespula maculata (White-face hornet)

<400> SEQUENCE: 91

Pro	Ile	Ile	Asn	Leu	Ser	Phe	Gly	Glu	Ala	Asn	Asn	Tyr	Cys	Lys	Ile				
1				5					10					15					
Lys	Cys	Ser	Arg	Gly	Ile	His	Thr	Leu	Cys	Lys	Phe	Gly	Thr	Ser	Met				
			20					25					30						
Lys	Pro	Asn	Cys	Gly	Ser	Lys	Leu	Val	Lys	Val	His	Gly	Val	Ser	Asn				

-continued

35	40	45
Asp Glu Lys Asn Glu Ile Val Asn Arg His Asn Gln Phe Arg Gln Lys 50 55 60		
Val Ala Lys Gly Leu Glu Thr Arg Gly Asn Pro Gly Pro Gln Pro Pro 65 70 75 80		
Ala Lys Asn Met Asn Val Leu Val Trp Asn Asp Glu Leu Ala Lys Ile 85 90 95		
Ala Gln Thr Trp Ala Asn Gln Cys Ser Phe Gly His Asp Gln Cys Arg 100 105 110		
Asn Thr Glu Lys Tyr Gln Val Gly Gln Asn Val Ala Ile Ala Ser Thr 115 120 125		
Thr Gly Asn Ser Tyr Ala Thr Met Ser Lys Leu Ile Glu Met Trp Glu 130 135 140		
Asn Glu Val Lys Asp Phe Asn Pro Lys Lys Gly Thr Met Gly Asp Asn 145 150 155 160		
Asn Phe Ser Lys Val Gly His Tyr Thr Gln Met Val Trp Gly Lys Thr 165 170 175		
Lys Glu Ile Gly Cys Gly Ser Val Lys Tyr Ile Glu Asn Asn Trp His 180 185 190		
Thr His Tyr Leu Val Cys Asn Tyr Gly Pro Ala Gly Asn Tyr Met Asp 195 200 205		
Gln Pro Ile Tyr Glu Arg Lys 210 215		

<210> SEQ ID NO 92

<211> LENGTH: 187

<212> TYPE: PRT

<213> ORGANISM: Equus caballus (Horse)

<400> SEQUENCE: 92

Met Lys Leu Leu Leu Leu Cys Leu Gly Leu Ile Leu Val Cys Ala Gln 1 5 10 15
Gln Glu Glu Asn Ser Asp Val Ala Ile Arg Asn Phe Asp Ile Ser Lys 20 25 30
Ile Ser Gly Glu Trp Tyr Ser Ile Phe Leu Ala Ser Asp Val Lys Glu 35 40 45
Lys Ile Glu Glu Asn Gly Ser Met Arg Val Phe Val Asp Val Ile Arg 50 55 60
Ala Leu Asp Asn Ser Ser Leu Tyr Ala Glu Tyr Gln Thr Lys Val Asn 65 70 75 80
Gly Glu Cys Thr Glu Phe Pro Met Val Phe Asp Lys Thr Glu Glu Asp 85 90 95
Gly Val Tyr Ser Leu Asn Tyr Asp Gly Tyr Asn Val Phe Arg Ile Ser 100 105 110
Glu Phe Glu Asn Asp Glu His Ile Ile Leu Tyr Leu Val Asn Phe Asp 115 120 125
Lys Asp Arg Pro Phe Gln Leu Phe Glu Phe Tyr Ala Arg Glu Pro Asp 130 135 140
Val Ser Pro Glu Ile Lys Glu Glu Phe Val Lys Ile Val Gln Lys Arg 145 150 155 160
Gly Ile Val Lys Glu Asn Ile Ile Asp Leu Thr Lys Ile Asp Arg Cys 165 170 175
Phe Gln Leu Arg Gly Asn Gly Val Ala Gln Ala 180 185

-continued

<210> SEQ ID NO 93
 <211> LENGTH: 29
 <212> TYPE: PRT
 <213> ORGANISM: Equus caballus (Horse)
 <220> FEATURE:
 <221> NAME/KEY: UNSURE
 <222> LOCATION: 3, 28
 <223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 93

Ser Gln Xaa Pro Gln Ser Glu Thr Asp Tyr Ser Gln Leu Ser Gly Glu
 1 5 10 15

Trp Asn Thr Ile Tyr Gly Ala Ala Ser Asn Ile Xaa Lys
 20 25

<210> SEQ ID NO 94
 <211> LENGTH: 19
 <212> TYPE: PRT
 <213> ORGANISM: Equus caballus (Horse)
 <220> FEATURE:
 <221> NAME/KEY: UNSURE
 <222> LOCATION: 1
 <223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 94

Xaa Gln Asp Pro Gln Ser Glu Thr Asp Tyr Ser Gln Leu Ser Gly Glu
 1 5 10 15

Trp Asn Thr

<210> SEQ ID NO 95
 <211> LENGTH: 211
 <212> TYPE: PRT
 <213> ORGANISM: Euroglyphus maynei (House-dust mite)

<400> SEQUENCE: 95

Thr Tyr Ala Cys Ser Ile Asn Ser Val Ser Leu Pro Ser Glu Leu Asp
 1 5 10 15

Leu Arg Ser Leu Arg Thr Val Thr Pro Ile Arg Met Gln Gly Gly Cys
 20 25 30

Gly Ser Cys Trp Ala Phe Ser Gly Val Ala Ser Thr Glu Ser Ala Tyr
 35 40 45

Leu Ala Tyr Arg Asn Met Ser Leu Asp Leu Ala Glu Gln Glu Leu Val
 50 55 60

Asp Cys Ala Ser Gln Asn Gly Cys His Gly Asp Thr Ile Pro Arg Gly
 65 70 75 80

Ile Glu Tyr Ile Gln Gln Asn Gly Val Val Gln Glu His Tyr Tyr Pro
 85 90 95

Tyr Val Ala Arg Glu Gln Ser Cys His Arg Pro Asn Ala Gln Arg Tyr
 100 105 110

Gly Leu Lys Asn Tyr Cys Gln Ile Ser Pro Pro Asp Ser Asn Lys Ile
 115 120 125

Arg Gln Ala Leu Thr Gln Thr His Thr Ala Val Ala Val Ile Ile Gly
 130 135 140

Ile Lys Asp Leu Asn Ala Phe Arg His Tyr Asp Gly Arg Thr Ile Met
 145 150 155 160

Gln His Asp Asn Gly Tyr Gln Pro Asn Tyr His Ala Val Asn Ile Val
 165 170 175

Gly Tyr Gly Asn Thr Gln Gly Val Asp Tyr Trp Ile Val Arg Asn Ser
 180 185 190

-continued

Trp Asp Thr Thr Trp Gly Asp Asn Gly Tyr Gly Tyr Phe Ala Ala Asn
195 200 205

Ile Asn Leu
210

<210> SEQ ID NO 96
<211> LENGTH: 92
<212> TYPE: PRT
<213> ORGANISM: Felis silvestris catus (Cat)

<400> SEQUENCE: 96

Met Lys Gly Ala Cys Val Leu Val Leu Leu Trp Ala Ala Leu Leu Leu
1 5 10 15
Ile Ser Gly Gly Asn Cys Glu Ile Cys Pro Ala Val Lys Arg Asp Val
20 25 30
Asp Leu Phe Leu Thr Gly Thr Pro Asp Glu Tyr Val Glu Gln Val Ala
35 40 45
Gln Tyr Lys Ala Leu Pro Val Val Leu Glu Asn Ala Arg Ile Leu Lys
50 55 60
Asn Cys Val Asp Ala Lys Met Thr Glu Glu Asp Lys Glu Asn Ala Leu
65 70 75 80
Ser Val Leu Asp Lys Ile Tyr Thr Ser Pro Leu Cys
85 90

<210> SEQ ID NO 97
<211> LENGTH: 88
<212> TYPE: PRT
<213> ORGANISM: Felis silvestris catus (Cat)

<400> SEQUENCE: 97

Met Leu Asp Ala Ala Leu Pro Pro Cys Pro Thr Val Ala Ala Thr Ala
1 5 10 15
Asp Cys Glu Ile Cys Pro Ala Val Lys Arg Asp Val Asp Leu Phe Leu
20 25 30
Thr Gly Thr Pro Asp Glu Tyr Val Glu Gln Val Ala Gln Tyr Lys Ala
35 40 45
Leu Pro Val Val Leu Glu Asn Ala Arg Ile Leu Lys Asn Cys Val Asp
50 55 60
Ala Lys Met Thr Glu Glu Asp Lys Glu Asn Ala Leu Ser Val Leu Asp
65 70 75 80
Lys Ile Tyr Thr Ser Pro Leu Cys
85

<210> SEQ ID NO 98
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Felis silvestris catus (Cat)

<400> SEQUENCE: 98

Met Arg Gly Ala Leu Leu Val Leu Ala Leu Leu Val Thr Gln Ala Leu
1 5 10 15
Gly Val Lys Met Ala Glu Thr Cys Pro Ile Phe Tyr Asp Val Phe Phe
20 25 30
Ala Val Ala Asn Gly Asn Glu Leu Leu Leu Asp Leu Ser Leu Thr Lys
35 40 45
Val Asn Ala Thr Glu Pro Glu Arg Thr Ala Met Lys Lys Ile Gln Asp
50 55 60
Cys Tyr Val Glu Asn Gly Leu Ile Ser Arg Val Leu Asp Gly Leu Val

-continued

65		70		75		80									
Met	Thr	Thr	Ile	Ser	Ser	Ser	Lys	Asp	Cys	Met	Gly	Glu	Ala	Val	Gln
			85						90					95	
Asn	Thr	Val	Glu	Asp	Leu	Lys	Leu	Asn	Thr	Leu	Gly	Arg			
			100					105							

<210> SEQ ID NO 99
 <211> LENGTH: 113
 <212> TYPE: PRT
 <213> ORGANISM: Gadus callarias (Baltic cod)

<400> SEQUENCE: 99

Ala	Phe	Lys	Gly	Ile	Leu	Ser	Asn	Ala	Asp	Ile	Lys	Ala	Ala	Glu	Ala
1				5					10					15	
Ala	Cys	Phe	Lys	Glu	Gly	Ser	Phe	Asp	Glu	Asp	Gly	Phe	Tyr	Ala	Lys
			20					25					30		
Val	Gly	Leu	Asp	Ala	Phe	Ser	Ala	Asp	Glu	Leu	Lys	Lys	Leu	Phe	Lys
			35				40					45			
Ile	Ala	Asp	Glu	Asp	Lys	Glu	Gly	Phe	Ile	Glu	Glu	Asp	Glu	Leu	Lys
			50			55					60				
Leu	Phe	Leu	Ile	Ala	Phe	Ala	Ala	Asp	Leu	Arg	Ala	Leu	Thr	Asp	Ala
65				70						75				80	
Glu	Thr	Lys	Ala	Phe	Leu	Lys	Ala	Gly	Asp	Ser	Asp	Gly	Asp	Gly	Lys
			85						90					95	
Ile	Gly	Val	Asp	Glu	Phe	Gly	Ala	Leu	Val	Asp	Lys	Trp	Gly	Ala	Lys
			100					105					110		

Gly

<210> SEQ ID NO 100
 <211> LENGTH: 210
 <212> TYPE: PRT
 <213> ORGANISM: Gallus gallus (Chicken)

<400> SEQUENCE: 100

Met	Ala	Met	Ala	Gly	Val	Phe	Val	Leu	Phe	Ser	Phe	Val	Leu	Cys	Gly
1				5					10					15	
Phe	Leu	Pro	Asp	Ala	Ala	Phe	Gly	Ala	Glu	Val	Asp	Cys	Ser	Arg	Phe
			20					25					30		
Pro	Asn	Ala	Thr	Asp	Lys	Glu	Gly	Lys	Asp	Val	Leu	Val	Cys	Asn	Lys
		35					40					45			
Asp	Leu	Arg	Pro	Ile	Cys	Gly	Thr	Asp	Gly	Val	Thr	Tyr	Thr	Asn	Asp
		50				55					60				
Cys	Leu	Leu	Cys	Ala	Tyr	Ser	Ile	Glu	Phe	Gly	Thr	Asn	Ile	Ser	Lys
65				70						75				80	
Glu	His	Asp	Gly	Glu	Cys	Lys	Glu	Thr	Val	Pro	Met	Asn	Cys	Ser	Ser
			85						90					95	
Tyr	Ala	Asn	Thr	Thr	Ser	Glu	Asp	Gly	Lys	Val	Met	Val	Leu	Cys	Asn
			100					105					110		
Arg	Ala	Phe	Asn	Pro	Val	Cys	Gly	Thr	Asp	Gly	Val	Thr	Tyr	Asp	Asn
		115					120					125			
Glu	Cys	Leu	Leu	Cys	Ala	His	Lys	Val	Glu	Gln	Gly	Ala	Ser	Val	Asp
		130				135					140				
Lys	Arg	His	Asp	Gly	Gly	Cys	Arg	Lys	Glu	Leu	Ala	Ala	Val	Ser	Val
145					150					155					160
Asp	Cys	Ser	Glu	Tyr	Pro	Lys	Pro	Asp	Cys	Thr	Ala	Glu	Asp	Arg	Pro
				165					170					175	

-continued

Leu Cys Gly Ser Asp Asn Lys Thr Tyr Gly Asn Lys Cys Asn Phe Cys
 180 185 190

Asn Ala Val Val Glu Ser Asn Gly Thr Leu Thr Leu Ser His Phe Gly
 195 200 205

Lys Cys
 210

<210> SEQ ID NO 101
 <211> LENGTH: 385
 <212> TYPE: PRT
 <213> ORGANISM: Gallus gallus (Chicken)

<400> SEQUENCE: 101

Gly Ser Ile Gly Ala Ala Ser Met Glu Phe Cys Phe Asp Val Phe Lys
 1 5 10 15

Glu Leu Lys Val His His Ala Asn Glu Asn Ile Phe Tyr Cys Pro Ile
 20 25 30

Ala Ile Met Ser Ala Leu Ala Met Val Tyr Leu Gly Ala Lys Asp Ser
 35 40 45

Thr Arg Thr Gln Ile Asn Lys Val Val Arg Phe Asp Lys Leu Pro Gly
 50 55 60

Phe Gly Asp Ser Ile Glu Ala Gln Cys Gly Thr Ser Val Asn Val His
 65 70 75 80

Ser Ser Leu Arg Asp Ile Leu Asn Gln Ile Thr Lys Pro Asn Asp Val
 85 90 95

Tyr Ser Phe Ser Leu Ala Ser Arg Leu Tyr Ala Glu Glu Arg Tyr Pro
 100 105 110

Ile Leu Pro Glu Tyr Leu Gln Cys Val Lys Glu Leu Tyr Arg Gly Gly
 115 120 125

Leu Glu Pro Ile Asn Phe Gln Thr Ala Ala Asp Gln Ala Arg Glu Leu
 130 135 140

Ile Asn Ser Trp Val Glu Ser Gln Thr Asn Gly Ile Ile Arg Asn Val
 145 150 155 160

Leu Gln Pro Ser Ser Val Asp Ser Gln Thr Ala Met Val Leu Val Asn
 165 170 175

Ala Ile Val Phe Lys Gly Leu Trp Glu Lys Ala Phe Lys Asp Glu Asp
 180 185 190

Thr Gln Ala Met Pro Phe Arg Val Thr Glu Gln Glu Ser Lys Pro Val
 195 200 205

Gln Met Met Tyr Gln Ile Gly Leu Phe Arg Val Ala Ser Met Ala Ser
 210 215 220

Glu Lys Met Lys Ile Leu Glu Leu Pro Phe Ala Ser Gly Thr Met Ser
 225 230 235 240

Met Leu Val Leu Leu Pro Asp Glu Val Ser Gly Leu Glu Gln Leu Glu
 245 250 255

Ser Ile Ile Asn Phe Glu Lys Leu Thr Glu Trp Thr Ser Ser Asn Val
 260 265 270

Met Glu Glu Arg Lys Ile Lys Val Tyr Leu Pro Arg Met Lys Met Glu
 275 280 285

Glu Lys Tyr Asn Leu Thr Ser Val Leu Met Ala Met Gly Ile Thr Asp
 290 295 300

Val Phe Ser Ser Ser Ala Asn Leu Ser Gly Ile Ser Ser Ala Glu Ser
 305 310 315 320

Leu Lys Ile Ser Gln Ala Val His Ala Ala His Ala Glu Ile Asn Glu

-continued

<210> SEQ ID NO 103
 <211> LENGTH: 147
 <212> TYPE: PRT
 <213> ORGANISM: Gallus gallus (Chicken)

<400> SEQUENCE: 103

Met Arg Ser Leu Leu Ile Leu Val Leu Cys Phe Leu Pro Leu Ala Ala
 1 5 10 15
 Leu Gly Lys Val Phe Gly Arg Cys Glu Leu Ala Ala Ala Met Lys Arg
 20 25 30
 His Gly Leu Asp Asn Tyr Arg Gly Tyr Ser Leu Gly Asn Trp Val Cys
 35 40 45
 Ala Ala Lys Phe Glu Ser Asn Phe Asn Thr Gln Ala Thr Asn Arg Asn
 50 55 60
 Thr Asp Gly Ser Thr Asp Tyr Gly Ile Leu Gln Ile Asn Ser Arg Trp
 65 70 75 80
 Trp Cys Asn Asp Gly Arg Thr Pro Gly Ser Arg Asn Leu Cys Asn Ile
 85 90 95
 Pro Cys Ser Ala Leu Leu Ser Ser Asp Ile Thr Ala Ser Val Asn Cys
 100 105 110
 Ala Lys Lys Ile Val Ser Asp Gly Asn Gly Met Asn Ala Trp Val Ala
 115 120 125
 Trp Arg Asn Arg Cys Lys Gly Thr Asp Val Gln Ala Trp Ile Arg Gly
 130 135 140
 Cys Arg Leu
 145

<210> SEQ ID NO 104
 <211> LENGTH: 133
 <212> TYPE: PRT
 <213> ORGANISM: Helianthus annuus (Common sunflower)

<400> SEQUENCE: 104

Met Ser Trp Gln Ala Tyr Val Asp Glu His Leu Met Cys Asp Ile Glu
 1 5 10 15
 Gly Thr Gly Gln His Leu Thr Ser Ala Ala Ile Leu Gly Leu Asp Gly
 20 25 30
 Thr Val Trp Ala Gln Ser Ala Lys Phe Pro Gln Phe Lys Pro Glu Glu
 35 40 45
 Met Lys Gly Ile Ile Lys Glu Phe Asp Glu Ala Gly Thr Leu Ala Pro
 50 55 60
 Thr Gly Met Phe Ile Ala Gly Ala Lys Tyr Met Val Leu Gln Gly Glu
 65 70 75 80
 Pro Gly Ala Val Ile Arg Gly Lys Lys Gly Ala Gly Gly Ile Cys Ile
 85 90 95
 Lys Lys Thr Gly Gln Ala Met Ile Met Gly Ile Tyr Asp Glu Pro Val
 100 105 110
 Ala Pro Gly Gln Cys Asn Met Val Val Glu Arg Leu Gly Asp Tyr Leu
 115 120 125
 Leu Glu Gln Gly Met
 130

<210> SEQ ID NO 105
 <211> LENGTH: 137
 <212> TYPE: PRT
 <213> ORGANISM: Hevea brasiliensis (Para rubber tree)

<400> SEQUENCE: 105

-continued

Ala Glu Asp Glu Asp Asn Gln Gln Gly Gln Gly Glu Gly Leu Lys Tyr
 1 5 10 15
 Leu Gly Phe Val Gln Asp Ala Ala Thr Tyr Ala Val Thr Thr Phe Ser
 20 25 30
 Asn Val Tyr Leu Phe Ala Lys Asp Lys Ser Gly Pro Leu Gln Pro Gly
 35 40 45
 Val Asp Ile Ile Glu Gly Pro Val Lys Asn Val Ala Val Pro Leu Tyr
 50 55 60
 Asn Arg Phe Ser Tyr Ile Pro Asn Gly Ala Leu Lys Phe Val Asp Ser
 65 70 75 80
 Thr Val Val Ala Ser Val Thr Ile Ile Asp Arg Ser Leu Pro Pro Ile
 85 90 95
 Val Lys Asp Ala Ser Ile Gln Val Val Ser Ala Ile Arg Ala Ala Pro
 100 105 110
 Glu Ala Ala Arg Ser Leu Ala Ser Ser Leu Pro Gly Gln Thr Lys Ile
 115 120 125
 Leu Ala Lys Val Phe Tyr Gly Glu Asn
 130 135

<210> SEQ ID NO 106
 <211> LENGTH: 150
 <212> TYPE: PRT
 <213> ORGANISM: Hevea brasiliensis (Para rubber tree)

<400> SEQUENCE: 106

Ala Ser Val Glu Val Glu Ser Ala Ala Thr Ala Leu Pro Lys Asn Glu
 1 5 10 15
 Thr Pro Glu Val Thr Lys Ala Glu Glu Thr Lys Thr Glu Glu Pro Ala
 20 25 30
 Ala Pro Pro Ala Ser Glu Gln Glu Thr Ala Asp Ala Thr Pro Glu Lys
 35 40 45
 Glu Glu Pro Thr Ala Ala Pro Ala Glu Pro Glu Ala Pro Ala Pro Glu
 50 55 60
 Thr Glu Lys Ala Glu Glu Val Glu Lys Ile Glu Lys Thr Glu Glu Pro
 65 70 75 80
 Ala Pro Glu Ala Asp Gln Thr Thr Pro Glu Glu Lys Pro Ala Glu Pro
 85 90 95
 Glu Pro Val Ala Glu Glu Glu Pro Lys His Glu Thr Lys Glu Thr Glu
 100 105 110
 Thr Glu Ala Pro Ala Ala Pro Ala Glu Gly Glu Lys Pro Ala Glu Glu
 115 120 125
 Glu Lys Pro Ile Thr Glu Ala Ala Glu Thr Ala Thr Thr Glu Val Pro
 130 135 140
 Val Glu Lys Thr Glu Glu
 145 150

<210> SEQ ID NO 107
 <211> LENGTH: 265
 <212> TYPE: PRT
 <213> ORGANISM: Holcus lanatus (Velvet grass)

<400> SEQUENCE: 107

Met Ala Ser Ser Ser Arg Ser Val Leu Leu Leu Val Ala Ala Leu Phe
 1 5 10 15
 Ala Val Phe Leu Gly Ser Ala His Gly Ile Ala Lys Val Pro Pro Gly
 20 25 30

-continued

Pro Asn Ile Thr Ala Thr Tyr Gly Asp Glu Trp Leu Asp Ala Lys Ser
 35 40 45
 Thr Trp Tyr Gly Lys Pro Thr Gly Ala Gly Pro Lys Asp Asn Gly Gly
 50 55 60
 Ala Cys Gly Tyr Lys Asp Val Asp Lys Pro Pro Phe Ser Gly Met Thr
 65 70 75 80
 Gly Cys Gly Asn Thr Pro Ile Phe Lys Asp Gly Arg Gly Cys Gly Ser
 85 90 95
 Cys Phe Glu Ile Lys Cys Thr Lys Pro Glu Ser Cys Ser Gly Glu Pro
 100 105 110
 Val Thr Val His Ile Thr Asp Asp Asn Glu Glu Pro Ile Ala Pro Tyr
 115 120 125
 His Phe Asp Leu Ser Gly His Ala Phe Gly Ser Met Ala Lys Lys Gly
 130 135 140
 Glu Glu Gln Lys Leu Arg Ser Ala Gly Glu Leu Glu Leu Lys Phe Arg
 145 150 155 160
 Arg Val Lys Cys Lys Tyr Pro Asp Gly Thr Lys Pro Thr Phe His Val
 165 170 175
 Glu Lys Gly Ser Asn Pro Asn Tyr Leu Ala Leu Leu Val Lys Tyr Ile
 180 185 190
 Asp Gly Asp Gly Asp Val Val Ala Val Asp Ile Lys Glu Lys Gly Lys
 195 200 205
 Asp Lys Trp Ile Glu Leu Lys Glu Ser Trp Gly Ala Val Trp Arg Val
 210 215 220
 Asp Thr Pro Asp Lys Leu Thr Gly Pro Phe Thr Val Arg Tyr Thr Thr
 225 230 235 240
 Glu Gly Gly Thr Lys Gly Glu Ala Glu Asp Val Ile Pro Glu Gly Trp
 245 250 255
 Lys Ala Asp Thr Ala Tyr Glu Ala Lys
 260 265

<210> SEQ ID NO 108

<211> LENGTH: 146

<212> TYPE: PRT

<213> ORGANISM: Hordeum vulgare (Barley)

<400> SEQUENCE: 108

Pro Thr Ser Val Ala Val Asp Gln Gly Ser Met Val Ser Asn Ser Pro
 1 5 10 15
 Gly Glu Trp Cys Trp Pro Gly Met Gly Tyr Pro Val Tyr Pro Phe Pro
 20 25 30
 Arg Cys Arg Ala Leu Val Lys Ser Gln Cys Ala Gly Gly Gln Val Val
 35 40 45
 Glu Ser Ile Gln Lys Asp Cys Cys Arg Gln Ile Ala Ala Ile Gly Asp
 50 55 60
 Glu Trp Cys Ile Cys Gly Ala Leu Gly Ser Met Arg Gly Ser Met Tyr
 65 70 75 80
 Lys Glu Leu Gly Val Ala Leu Ala Asp Asp Lys Ala Thr Val Ala Glu
 85 90 95
 Val Phe Pro Gly Cys Arg Thr Glu Val Met Asp Arg Ala Val Ala Ser
 100 105 110
 Leu Pro Ala Val Cys Asn Gln Tyr Ile Pro Asn Thr Asn Gly Thr Asp
 115 120 125
 Gly Val Cys Tyr Trp Leu Ser Tyr Tyr Gln Pro Pro Arg Gln Met Ser

-continued

Gly Asn Ala Ala Pro Gln Leu Thr Lys Asn Ala Gly Val Val Thr
 355 360 365

<210> SEQ ID NO 110
 <211> LENGTH: 225
 <212> TYPE: PRT
 <213> ORGANISM: Juniperus ashei (Ozark white cedar)

<400> SEQUENCE: 110

Met Ala Arg Val Ser Glu Leu Ala Phe Leu Leu Ala Ala Thr Leu Ala
 1 5 10 15
 Ile Ser Leu His Met Gln Glu Ala Gly Val Val Lys Phe Asp Ile Lys
 20 25 30
 Asn Gln Cys Gly Tyr Thr Val Trp Ala Ala Gly Leu Pro Gly Gly Gly
 35 40 45
 Lys Arg Leu Asp Gln Gly Gln Thr Trp Thr Val Asn Leu Ala Ala Gly
 50 55 60
 Thr Ala Ser Ala Arg Phe Trp Gly Arg Thr Gly Cys Thr Phe Asp Ala
 65 70 75 80
 Ser Gly Lys Gly Ser Cys Gln Thr Gly Asp Cys Gly Gly Gln Leu Ser
 85 90 95
 Cys Thr Val Ser Gly Ala Val Pro Ala Thr Leu Ala Glu Tyr Thr Gln
 100 105 110
 Ser Asp Gln Asp Tyr Tyr Asp Val Ser Leu Val Asp Gly Phe Asn Ile
 115 120 125
 Pro Leu Ala Ile Asn Pro Thr Asn Ala Gln Cys Thr Ala Pro Ala Cys
 130 135 140
 Lys Ala Asp Ile Asn Ala Val Cys Pro Ser Glu Leu Lys Val Asp Gly
 145 150 155 160
 Gly Cys Asn Ser Ala Cys Asn Val Phe Lys Thr Asp Gln Tyr Cys Cys
 165 170 175
 Arg Asn Ala Tyr Val Asp Asn Cys Pro Ala Thr Asn Tyr Ser Lys Ile
 180 185 190
 Phe Lys Asn Gln Cys Pro Gln Ala Tyr Ser Tyr Ala Lys Asp Asp Thr
 195 200 205
 Ala Thr Phe Ala Cys Ala Ser Gly Thr Asp Tyr Ser Ile Val Phe Cys
 210 215 220
 Pro
 225

<210> SEQ ID NO 111
 <211> LENGTH: 141
 <212> TYPE: PRT
 <213> ORGANISM: Lepidoglyphus destructor (Storage mite)

<400> SEQUENCE: 111

Met Met Lys Phe Ile Ala Leu Phe Ala Leu Val Ala Val Ala Ser Ala
 1 5 10 15
 Gly Lys Met Thr Phe Lys Asp Cys Gly His Gly Glu Val Thr Glu Leu
 20 25 30
 Asp Ile Thr Gly Cys Ser Gly Asp Thr Cys Val Ile His Arg Gly Glu
 35 40 45
 Lys Met Thr Leu Glu Ala Lys Phe Ala Ala Asn Gln Asp Thr Ala Lys
 50 55 60
 Val Thr Ile Lys Val Leu Ala Lys Val Ala Gly Thr Thr Ile Gln Val
 65 70 75 80

-continued

Ala Ala Pro Val Glu Phe Thr Val Glu Lys Gly Ser Asp Glu Lys Asn
 1 5 10 15
 Leu Ala Leu Ser Ile Lys Tyr Asn Lys Glu Gly Asp Ser Met Ala Glu
 20 25 30
 Val Glu Leu Lys Glu His Gly Ser Asn Glu Trp Leu Ala Leu Lys Lys
 35 40 45
 Asn Gly Asp Gly Val Trp Glu Ile Lys Ser Asp Lys Pro Leu Lys Gly
 50 55 60
 Pro Phe Asn Phe Arg Phe Val Ser Glu Lys Gly Met Arg Asn Val Phe
 65 70 75 80
 Asp Asp Val Val Pro Ala Asp Phe Lys Val Gly Thr Thr Tyr Lys Pro
 85 90 95
 Glu

<210> SEQ ID NO 114
 <211> LENGTH: 97
 <212> TYPE: PRT
 <213> ORGANISM: Lolium perenne (Perennial ryegrass)

<400> SEQUENCE: 114

Thr Lys Val Asp Leu Thr Val Glu Lys Gly Ser Asp Ala Lys Thr Leu
 1 5 10 15
 Val Leu Asn Ile Lys Tyr Thr Arg Pro Gly Asp Thr Leu Ala Glu Val
 20 25 30
 Glu Leu Arg Gln His Gly Ser Glu Glu Trp Glu Pro Met Thr Lys Lys
 35 40 45
 Gly Asn Leu Trp Glu Val Lys Ser Ala Lys Pro Leu Thr Gly Pro Met
 50 55 60
 Asn Phe Arg Phe Leu Ser Lys Gly Gly Met Lys Asn Val Phe Asp Glu
 65 70 75 80
 Val Ile Pro Thr Ala Phe Thr Val Gly Lys Thr Tyr Thr Pro Glu Tyr
 85 90 95

Asn

<210> SEQ ID NO 115
 <211> LENGTH: 308
 <212> TYPE: PRT
 <213> ORGANISM: Lolium perenne (Perennial ryegrass)

<400> SEQUENCE: 115

Met Ala Val Gln Lys Tyr Thr Val Ala Leu Phe Leu Arg Arg Gly Pro
 1 5 10 15
 Arg Gly Gly Pro Gly Arg Ser Tyr Ala Ala Asp Ala Gly Tyr Thr Pro
 20 25 30
 Ala Ala Ala Ala Thr Pro Ala Thr Pro Ala Ala Thr Pro Ala Gly Gly
 35 40 45
 Trp Arg Glu Gly Asp Asp Arg Arg Ala Glu Ala Ala Gly Gly Arg Gln
 50 55 60
 Arg Leu Ala Ser Arg Gln Pro Trp Pro Pro Leu Pro Thr Pro Leu Arg
 65 70 75 80
 Arg Thr Ser Ser Arg Ser Ser Arg Pro Pro Ser Pro Ser Pro Pro Arg
 85 90 95
 Ala Ser Ser Pro Thr Ser Ala Ala Lys Ala Pro Gly Leu Ile Pro Lys
 100 105 110
 Leu Asp Thr Ala Tyr Asp Val Ala Tyr Lys Ala Ala Glu Ala His Pro
 115 120 125

-continued

Arg Gly Gln Val Arg Arg Leu Arg His Cys Pro His Arg Ser Leu Arg
 130 135 140
 Val Ile Ala Gly Ala Leu Glu Val His Ala Val Lys Pro Ala Thr Glu
 145 150 155 160
 Glu Val Leu Ala Ala Lys Ile Pro Thr Gly Glu Leu Gln Ile Val Asp
 165 170 175
 Lys Ile Asp Ala Ala Phe Lys Ile Ala Ala Thr Ala Ala Asn Ala Ala
 180 185 190
 Pro Thr Asn Asp Lys Phe Thr Val Phe Glu Ser Ala Phe Asn Lys Ala
 195 200 205
 Leu Asn Glu Cys Thr Gly Gly Ala Met Arg Pro Thr Ser Ser Ser Pro
 210 215 220
 Pro Ser Arg Pro Arg Ser Ser Arg Pro Thr Pro Pro Pro Ser Pro Ala
 225 230 235 240
 Ala Pro Glu Val Lys Tyr Ala Val Phe Glu Ala Ala Leu Thr Lys Ala
 245 250 255
 Ile Thr Ala Met Thr Gln Ala Gln Lys Ala Gly Lys Pro Ala Ala Ala
 260 265 270
 Ala Ala Thr Ala Ala Ala Thr Val Ala Thr Ala Ala Ala Thr Ala Ala
 275 280 285
 Ala Val Leu Pro Pro Pro Leu Leu Val Val Gln Ser Leu Ile Ser Leu
 290 295 300
 Leu Ile Tyr Tyr
 305

<210> SEQ ID NO 116
 <211> LENGTH: 339
 <212> TYPE: PRT
 <213> ORGANISM: Lolium perenne (Perennial ryegrass)

<400> SEQUENCE: 116

Met Ala Val Gln Lys His Thr Val Ala Leu Phe Leu Ala Val Ala Leu
 1 5 10 15
 Val Ala Gly Pro Ala Ala Ser Tyr Ala Ala Asp Ala Gly Tyr Ala Pro
 20 25 30
 Ala Thr Pro Ala Thr Pro Ala Ala Pro Ala Thr Ala Ala Thr Pro Ala
 35 40 45
 Thr Pro Ala Thr Pro Ala Thr Pro Ala Ala Val Pro Ser Gly Lys Ala
 50 55 60
 Thr Thr Glu Glu Gln Lys Leu Ile Glu Lys Ile Asn Ala Gly Phe Lys
 65 70 75 80
 Ala Ala Val Ala Ala Ala Ala Val Val Pro Pro Ala Asp Lys Tyr Lys
 85 90 95
 Thr Phe Val Glu Thr Phe Gly Thr Ala Thr Asn Lys Ala Phe Val Glu
 100 105 110
 Gly Leu Ala Ser Gly Tyr Ala Asp Gln Ser Lys Asn Gln Leu Thr Ser
 115 120 125
 Lys Leu Asp Ala Ala Leu Lys Leu Ala Tyr Glu Ala Ala Gln Gly Ala
 130 135 140
 Thr Pro Glu Ala Lys Tyr Asp Ala Tyr Val Ala Thr Leu Thr Glu Ala
 145 150 155 160
 Leu Arg Val Ile Ala Gly Thr Leu Glu Val His Ala Val Lys Pro Ala
 165 170 175
 Ala Glu Glu Val Lys Val Gly Ala Ile Pro Ala Ala Glu Val Gln Leu

-continued

180				185				190							
Ile	Asp	Lys	Val	Asp	Ala	Ala	Tyr	Arg	Thr	Ala	Ala	Thr	Ala	Ala	Asn
	195						200					205			
Ala	Ala	Pro	Ala	Asn	Asp	Lys	Phe	Thr	Val	Phe	Glu	Asn	Thr	Phe	Asn
	210					215					220				
Asn	Ala	Ile	Lys	Val	Ser	Leu	Gly	Ala	Ala	Tyr	Asp	Ser	Tyr	Lys	Phe
225					230					235					240
Ile	Pro	Thr	Leu	Val	Ala	Ala	Val	Lys	Gln	Ala	Tyr	Ala	Ala	Lys	Gln
			245						250					255	
Ala	Thr	Ala	Pro	Glu	Val	Lys	Tyr	Thr	Val	Ser	Glu	Thr	Ala	Leu	Lys
			260						265					270	
Lys	Ala	Val	Thr	Ala	Met	Ser	Glu	Ala	Glu	Lys	Glu	Ala	Thr	Pro	Ala
		275					280						285		
Ala	Ala	Ala	Thr	Ala	Thr	Pro	Thr	Pro	Ala	Ala	Ala	Thr	Ala	Thr	Ala
		290				295					300				
Thr	Pro	Ala	Ala	Ala	Tyr	Ala	Thr	Ala	Thr	Pro	Ala	Ala	Ala	Thr	Ala
305					310					315					320
Thr	Ala	Thr	Pro	Ala	Ala	Ala	Thr	Ala	Thr	Pro	Ala	Ala	Ala	Gly	Gly
			325						330					335	

Tyr Lys Val

<210> SEQ ID NO 117
 <211> LENGTH: 158
 <212> TYPE: PRT
 <213> ORGANISM: Malus domestica (Apple) (Malus sylvestris)
 <400> SEQUENCE: 117

Gly	Val	Tyr	Thr	Phe	Glu	Asn	Glu	Phe	Thr	Ser	Glu	Ile	Pro	Pro	Ser
1				5					10				15		
Arg	Leu	Phe	Lys	Ala	Phe	Val	Leu	Asp	Ala	Asp	Asn	Leu	Ile	Pro	Lys
		20						25					30		
Ile	Ala	Pro	Gln	Ala	Ile	Lys	Gln	Ala	Glu	Ile	Leu	Glu	Gly	Asn	Gly
		35					40					45			
Gly	Pro	Gly	Thr	Ile	Lys	Lys	Ile	Thr	Phe	Gly	Glu	Gly	Ser	Gln	Tyr
	50					55					60				
Gly	Tyr	Val	Lys	His	Arg	Ile	Asp	Ser	Ile	Asp	Glu	Ala	Ser	Tyr	Ser
65					70					75					80
Tyr	Ser	Tyr	Thr	Leu	Ile	Glu	Gly	Asp	Ala	Leu	Thr	Asp	Thr	Ile	Glu
			85						90					95	
Lys	Ile	Ser	Tyr	Glu	Thr	Lys	Leu	Val	Ala	Cys	Gly	Ser	Gly	Ser	Thr
		100					105						110		
Ile	Lys	Ser	Ile	Ser	His	Tyr	His	Thr	Lys	Gly	Asn	Ile	Glu	Ile	Lys
		115					120					125			
Glu	Glu	His	Val	Lys	Val	Gly	Lys	Glu	Lys	Ala	His	Gly	Leu	Phe	Lys
		130				135					140				
Leu	Ile	Glu	Ser	Tyr	Leu	Lys	Asp	His	Pro	Asp	Ala	Tyr	Asn		
145					150					155					

<210> SEQ ID NO 118
 <211> LENGTH: 133
 <212> TYPE: PRT
 <213> ORGANISM: Mercurialis annua (Annual mercury)

<400> SEQUENCE: 118

Met	Ser	Trp	Gln	Thr	Tyr	Val	Asp	Asp	His	Leu	Met	Cys	Asp	Ile	Asp
1					5				10					15	

-continued

Gly Gln Gly Gln His Leu Ala Ala Ala Ser Ile Val Gly His Asp Gly
 20 25 30
 Ser Ile Trp Ala Gln Ser Ala Ser Phe Pro Gln Leu Lys Pro Glu Glu
 35 40 45
 Ile Thr Gly Ile Met Lys Asp Phe Asp Glu Pro Gly His Leu Ala Pro
 50 55 60
 Thr Gly Leu Tyr Ile Ala Gly Thr Lys Tyr Met Val Ile Gln Gly Glu
 65 70 75 80
 Ser Gly Ala Val Ile Arg Gly Lys Lys Gly Ser Gly Gly Ile Thr Ile
 85 90 95
 Lys Lys Thr Gly Gln Ala Leu Val Phe Gly Ile Tyr Glu Glu Pro Val
 100 105 110
 Thr Pro Gly Gln Cys Asn Met Val Val Glu Arg Leu Gly Asp Tyr Leu
 115 120 125
 Ile Glu Gln Gly Met
 130

<210> SEQ ID NO 119

<211> LENGTH: 274

<212> TYPE: PRT

<213> ORGANISM: Metapenaeus ensis (Greasyback shrimp) (Sand shrim

<400> SEQUENCE: 119

Met Lys Leu Glu Lys Asp Asn Ala Met Asp Arg Ala Asp Thr Leu Glu
 1 5 10 15
 Gln Gln Asn Lys Glu Ala Asn Asn Arg Ala Glu Lys Ser Glu Glu Glu
 20 25 30
 Val His Asn Leu Gln Lys Arg Met Gln Gln Leu Glu Asn Asp Leu Asp
 35 40 45
 Gln Val Gln Glu Ser Leu Leu Lys Ala Asn Asn Gln Leu Val Glu Lys
 50 55 60
 Asp Lys Ala Leu Ser Asn Ala Glu Gly Glu Val Ala Ala Leu Asn Arg
 65 70 75 80
 Arg Ile Gln Leu Leu Glu Glu Asp Leu Glu Arg Ser Glu Glu Arg Leu
 85 90 95
 Asn Thr Ala Thr Thr Lys Leu Ala Glu Ala Ser Gln Ala Ala Asp Glu
 100 105 110
 Ser Glu Arg Met Arg Lys Val Leu Glu Asn Arg Ser Leu Ser Asp Glu
 115 120 125
 Glu Arg Met Asp Ala Leu Glu Asn Gln Leu Lys Glu Ala Arg Phe Leu
 130 135 140
 Ala Glu Glu Ala Asp Arg Lys Tyr Asp Glu Val Ala Arg Lys Leu Ala
 145 150 155 160
 Met Val Glu Ala Asp Leu Glu Arg Ala Glu Glu Arg Ala Glu Thr Gly
 165 170 175
 Glu Ser Lys Ile Val Glu Leu Glu Glu Glu Leu Arg Val Val Gly Asn
 180 185 190
 Asn Leu Lys Ser Leu Glu Val Ser Glu Glu Lys Ala Asn Gln Arg Glu
 195 200 205
 Glu Ala Tyr Lys Glu Gln Ile Lys Thr Leu Thr Asn Lys Leu Lys Ala
 210 215 220
 Ala Glu Ala Arg Ala Glu Phe Ala Glu Arg Ser Val Gln Lys Leu Gln
 225 230 235 240
 Lys Glu Val Asp Arg Leu Glu Asp Glu Leu Val Asn Glu Lys Glu Lys

-continued

	245		250		255										
Tyr	Lys	Ser	Ile	Thr	Asp	Glu	Leu	Asp	Gln	Thr	Phe	Ser	Glu	Leu	Ser
			260					265					270		

Gly Tyr

<210> SEQ ID NO 120
 <211> LENGTH: 180
 <212> TYPE: PRT
 <213> ORGANISM: Mus musculus (Mouse)

<400> SEQUENCE: 120

Met	Lys	Met	Leu	Leu	Leu	Leu	Cys	Leu	Gly	Leu	Thr	Leu	Val	Cys	Val
1				5					10					15	
His	Ala	Glu	Glu	Ala	Ser	Ser	Thr	Gly	Arg	Asn	Phe	Asn	Val	Glu	Lys
			20					25					30		
Ile	Asn	Gly	Glu	Trp	His	Thr	Ile	Ile	Leu	Ala	Ser	Asp	Lys	Arg	Glu
		35					40					45			
Lys	Ile	Glu	Asp	Asn	Gly	Asn	Phe	Arg	Leu	Phe	Leu	Glu	Gln	Ile	His
	50					55					60				
Val	Leu	Glu	Asn	Ser	Leu	Val	Leu	Lys	Phe	His	Thr	Val	Arg	Asp	Glu
65					70					75					80
Glu	Cys	Ser	Glu	Leu	Ser	Met	Val	Ala	Asp	Lys	Thr	Glu	Lys	Ala	Gly
				85					90					95	
Glu	Tyr	Ser	Val	Thr	Tyr	Asp	Gly	Phe	Asn	Thr	Phe	Thr	Ile	Pro	Lys
			100					105					110		
Thr	Asp	Tyr	Asp	Asn	Phe	Leu	Met	Ala	His	Leu	Ile	Asn	Glu	Lys	Asp
		115					120						125		
Gly	Glu	Thr	Phe	Gln	Leu	Met	Gly	Leu	Tyr	Gly	Arg	Glu	Pro	Asp	Leu
		130				135					140				
Met	Ser	Asp	Ile	Lys	Glu	Arg	Phe	Ala	Gln	Leu	Cys	Glu	Glu	His	Gly
145					150					155					160
Ile	Leu	Arg	Glu	Asn	Ile	Ile	Asp	Leu	Ser	Asn	Ala	Asn	Arg	Cys	Leu
				165					170					175	
Gln	Ala	Arg	Glu												
			180												

<210> SEQ ID NO 121
 <211> LENGTH: 112
 <212> TYPE: PRT
 <213> ORGANISM: Myrmecia pilosula (Bulldog ant) (Australian jumpe

<400> SEQUENCE: 121

Met	Lys	Leu	Ser	Cys	Leu	Leu	Leu	Thr	Leu	Thr	Ile	Ile	Phe	Val	Leu
1				5					10					15	
Thr	Ile	Val	His	Ala	Pro	Asn	Val	Glu	Ala	Lys	Asp	Leu	Ala	Asp	Pro
			20					25					30		
Glu	Ser	Glu	Ala	Val	Gly	Phe	Ala	Asp	Ala	Phe	Gly	Glu	Ala	Asp	Ala
		35					40					45			
Val	Gly	Glu	Ala	Asp	Pro	Asn	Ala	Gly	Leu	Gly	Ser	Val	Phe	Gly	Arg
	50					55					60				
Leu	Ala	Arg	Ile	Leu	Gly	Arg	Val	Ile	Pro	Lys	Val	Ala	Lys	Lys	Leu
65					70					75					80
Gly	Pro	Lys	Val	Ala	Lys	Val	Leu	Pro	Lys	Val	Met	Lys	Glu	Ala	Ile
			85					90						95	
Pro	Met	Ala	Val	Glu	Met	Ala	Lys	Ser	Gln	Glu	Glu	Gln	Gln	Pro	Gln
			100					105						110	

-continued

<210> SEQ ID NO 122
 <211> LENGTH: 75
 <212> TYPE: PRT
 <213> ORGANISM: Myrmecia pilosula (Bulldog ant) (Australian jumpe

<400> SEQUENCE: 122

Met Lys Leu Ser Cys Leu Leu Leu Thr Leu Ala Ile Ile Phe Val Leu
 1 5 10 15
 Thr Ile Val His Ala Pro Asn Val Glu Ala Lys Ala Leu Ala Asp Pro
 20 25 30
 Glu Ser Asp Ala Val Gly Phe Ala Asp Ala Val Gly Glu Ala Asp Pro
 35 40 45
 Ile Asp Trp Lys Lys Val Asp Trp Lys Lys Val Ser Lys Lys Thr Cys
 50 55 60
 Lys Val Met Leu Lys Ala Cys Lys Phe Leu Gly
 65 70 75

<210> SEQ ID NO 123
 <211> LENGTH: 145
 <212> TYPE: PRT
 <213> ORGANISM: Olea europaea (Common olive)

<400> SEQUENCE: 123

Glu Asp Ile Pro Gln Pro Pro Val Ser Gln Phe His Ile Gln Gly Gln
 1 5 10 15
 Val Tyr Cys Asp Thr Cys Arg Ala Gly Phe Ile Thr Glu Leu Ser Glu
 20 25 30
 Phe Ile Pro Gly Ala Ser Leu Arg Leu Gln Cys Lys Asp Lys Glu Asn
 35 40 45
 Gly Asp Val Thr Phe Thr Glu Val Gly Tyr Thr Arg Ala Glu Gly Leu
 50 55 60
 Tyr Ser Met Leu Val Glu Arg Asp His Lys Asn Glu Phe Cys Glu Ile
 65 70 75 80
 Thr Leu Ile Ser Ser Gly Arg Lys Asp Cys Asn Glu Ile Pro Thr Glu
 85 90 95
 Gly Trp Ala Lys Pro Ser Leu Lys Phe Lys Leu Asn Thr Val Asn Gly
 100 105 110
 Thr Thr Arg Thr Val Asn Pro Leu Gly Phe Phe Lys Lys Glu Ala Leu
 115 120 125
 Pro Lys Cys Ala Gln Val Tyr Asn Lys Leu Gly Met Tyr Pro Pro Asn
 130 135 140
 Met
 145

<210> SEQ ID NO 124
 <211> LENGTH: 24
 <212> TYPE: PRT
 <213> ORGANISM: Olea europaea (Common olive)

<400> SEQUENCE: 124

Ala Phe Ala Asn Thr Gly Val Glu Ile Val Ser Ile Asp Thr Tyr Leu
 1 5 10 15
 Phe Ser Leu Tyr Asp Glu Asp Lys
 20

<210> SEQ ID NO 125
 <211> LENGTH: 29

-continued

<212> TYPE: PRT

<213> ORGANISM: Olea europaea (Common olive)

<400> SEQUENCE: 125

Val Lys Ala Val Thr Val Leu Asn Ser Ser Glu Gly Pro His Gly Ile
1 5 10 15Val Tyr Phe Ala Gln Glu Gly Asp Gly Pro Thr Thr Val
20 25

<210> SEQ ID NO 126

<211> LENGTH: 19

<212> TYPE: PRT

<213> ORGANISM: Olea europaea (Common olive)

<220> FEATURE:

<221> NAME/KEY: UNSURE

<222> LOCATION: 14, 16

<223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 126

Ala Pro Ser Gln Gly Thr Val Thr Ala Lys Leu Thr Ser Xaa Val Xaa
1 5 10 15

Tyr Lys Asp

<210> SEQ ID NO 127

<211> LENGTH: 263

<212> TYPE: PRT

<213> ORGANISM: Oryza sativa (Rice)

<400> SEQUENCE: 127

Met Ala Ser Ser Ser Leu Leu Leu Ala Cys Val Val Val Ala Ala Met
1 5 10 15Val Ser Pro Ser Pro Ala Gly His Pro Lys Val Pro Pro Gly Pro Asn
20 25 30Ile Thr Thr Ser Tyr Gly Asp Lys Trp Leu Glu Ala Arg Pro Pro Gly
35 40 45Met Val Arg Pro Arg Val Leu Ala Pro Lys Asp Asn Gly Gly Ala Cys
50 55 60Gly Tyr Lys Asp Val Asp Lys Ala Pro Phe Leu Gly Met Asn Ser Cys
65 70 75 80Gly Asn Asp Pro Ile Phe Lys Asp Gly Lys Gly Cys Gly Ser Cys Phe
85 90 95Glu Ile Lys Cys Ser Lys Pro Glu Ala Cys Ser Asp Lys Pro Ala Leu
100 105 110Ile His Val Thr Asp Met Asn Asp Glu Pro Ile Ala Ala Tyr His Phe
115 120 125Asp Leu Ser Gly Leu Ala Met Ala Lys Asp Gly Lys Asp Glu Glu Leu
130 135 140Arg Lys Ala Gly Ile Ile Asp Thr Gln Phe Arg Arg Val Lys Cys Lys
145 150 155 160Tyr Pro Ala Asp Thr Lys Ile Thr Phe His Ile Glu Lys Ala Ser Asn
165 170 175Pro Asn Tyr Leu Ala Leu Leu Val Lys Tyr Val Ala Gly Asp Gly Asp
180 185 190Val Val Glu Val Glu Ile Lys Glu Lys Gly Ser Glu Glu Trp Lys Ala
195 200 205Leu Lys Glu Ser Trp Gly Ala Ile Trp Arg Ile Asp Thr Pro Lys Pro
210 215 220

Leu Lys Gly Pro Phe Ser Val Arg Val Thr Thr Glu Gly Ala Arg Arg

-continued

```

225                230                235                240
Ser Ser Ala Glu Asp Ala Ile Pro Asp Pro Gly Arg Arg Gln Arg Val
                245                250                255

Gln Val Asn Val Gln Ala Lys
                260

```

```

<210> SEQ ID NO 128
<211> LENGTH: 139
<212> TYPE: PRT
<213> ORGANISM: Parietaria judaica

```

```

<400> SEQUENCE: 128

```

```

Gln Glu Thr Cys Gly Thr Met Val Arg Ala Leu Met Pro Cys Leu Pro
 1                    5                    10                    15
Phe Val Gln Gly Lys Glu Lys Glu Pro Ser Lys Gly Cys Cys Ser Gly
                20                    25                    30
Ala Lys Arg Leu Asp Gly Glu Thr Lys Thr Gly Pro Gln Arg Val His
                35                    40                    45
Ala Cys Glu Cys Ile Gln Thr Ala Met Lys Thr Tyr Ser Asp Ile Asp
 50                    55                    60
Gly Lys Leu Val Ser Glu Val Pro Lys His Cys Gly Ile Val Asp Ser
65                    70                    75                    80
Lys Leu Pro Pro Ile Asp Val Asn Met Asp Cys Lys Thr Val Gly Val
                85                    90                    95
Val Pro Arg Gln Pro Gln Leu Pro Val Ser Leu Arg His Gly Pro Val
                100                   105                   110
Thr Gly Pro Ser Asp Pro Ala His Lys Ala Arg Leu Glu Arg Pro Gln
                115                   120                   125
Ile Arg Val Pro Pro Pro Ala Pro Glu Lys Ala
                130                   135

```

```

<210> SEQ ID NO 129
<211> LENGTH: 176
<212> TYPE: PRT
<213> ORGANISM: Parietaria judaica

```

```

<400> SEQUENCE: 129

```

```

Met Arg Thr Val Ser Ala Pro Ser Ala Val Ala Leu Val Val Ile Val
 1                    5                    10                    15
Ala Ala Gly Leu Ala Trp Thr Ser Leu Ala Ser Val Ala Pro Pro Ala
                20                    25                    30
Pro Ala Pro Gly Ser Glu Glu Thr Cys Gly Thr Val Val Arg Ala Leu
                35                    40                    45
Met Pro Cys Leu Pro Phe Val Gln Gly Lys Glu Lys Glu Pro Ser Lys
 50                    55                    60
Gly Cys Cys Ser Gly Ala Lys Arg Leu Asp Gly Glu Thr Lys Thr Gly
65                    70                    75                    80
Leu Gln Arg Val His Ala Cys Glu Cys Ile Gln Thr Ala Met Lys Thr
                85                    90                    95
Tyr Ser Asp Ile Asp Gly Lys Leu Val Ser Glu Val Pro Lys His Cys
                100                   105                   110
Gly Ile Val Asp Ser Lys Leu Pro Pro Ile Asp Val Asn Met Asp Cys
                115                   120                   125
Lys Thr Leu Gly Val Val Pro Arg Gln Pro Gln Leu Pro Val Ser Leu
                130                   135                   140
Arg His Gly Pro Val Thr Gly Pro Ser Asp Pro Ala His Lys Ala Arg

```

-continued

145	150	155	160
Leu Glu Arg Pro Gln Ile Arg Val Pro Pro Pro Ala Pro Glu Lys Ala			
	165	170	175

<210> SEQ ID NO 130
 <211> LENGTH: 138
 <212> TYPE: PRT
 <213> ORGANISM: Parietaria judaica

<400> SEQUENCE: 130

Met Arg Thr Val Ser Ala Arg Ser Ser Val Ala Leu Val Val Ile Val			
1	5	10	15
Ala Ala Val Leu Val Trp Thr Ser Ser Ala Ser Val Ala Pro Ala Pro			
	20	25	30
Ala Pro Gly Ser Glu Glu Thr Cys Gly Thr Val Val Gly Ala Leu Met			
	35	40	45
Pro Cys Leu Pro Phe Val Gln Gly Lys Glu Lys Glu Pro Ser Lys Gly			
	50	55	60
Cys Cys Ser Gly Ala Lys Arg Leu Asp Gly Glu Thr Lys Thr Gly Pro			
65	70	75	80
Gln Arg Val His Ala Cys Glu Cys Ile Gln Thr Ala Met Lys Thr Tyr			
	85	90	95
Ser Asp Ile Asp Gly Lys Leu Val Ser Glu Val Pro Lys His Cys Gly			
	100	105	110
Ile Val Asp Ser Lys Leu Pro Pro Ile Asp Val Asn Met Asp Cys Lys			
	115	120	125
Thr Leu Gly Val Leu His Tyr Lys Gly Asn			
	130	135	

<210> SEQ ID NO 131
 <211> LENGTH: 133
 <212> TYPE: PRT
 <213> ORGANISM: Parietaria judaica

<400> SEQUENCE: 131

Met Arg Thr Val Ser Met Ala Ala Leu Val Val Ile Ala Ala Ala Leu			
1	5	10	15
Ala Trp Thr Ser Ser Ala Glu Pro Ala Pro Ala Pro Ala Pro Gly Glu			
	20	25	30
Glu Ala Cys Gly Lys Val Val Gln Asp Ile Met Pro Cys Leu His Phe			
	35	40	45
Val Lys Gly Glu Glu Lys Glu Pro Ser Lys Glu Cys Cys Ser Gly Thr			
	50	55	60
Lys Lys Leu Ser Glu Glu Val Lys Thr Thr Glu Gln Lys Arg Glu Ala			
65	70	75	80
Cys Lys Cys Ile Val Arg Ala Thr Lys Gly Ile Ser Gly Ile Lys Asn			
	85	90	95
Glu Leu Val Ala Glu Val Pro Lys Lys Cys Asp Ile Lys Thr Thr Leu			
	100	105	110
Pro Pro Ile Thr Ala Asp Phe Asp Cys Ser Lys Ile Gln Ser Thr Ile			
	115	120	125
Phe Arg Gly Tyr Tyr			
	130		

<210> SEQ ID NO 132
 <211> LENGTH: 133
 <212> TYPE: PRT

-continued

<213> ORGANISM: *Parietaria judaica*

<400> SEQUENCE: 132

Met Arg Thr Val Ser Met Ala Ala Leu Val Val Ile Ala Ala Ala Leu
 1 5 10 15
 Ala Trp Thr Ser Ser Ala Glu Leu Ala Ser Ala Pro Ala Pro Gly Glu
 20 25 30
 Gly Pro Cys Gly Lys Val Val His His Ile Met Pro Cys Leu Lys Phe
 35 40 45
 Val Lys Gly Glu Glu Lys Glu Pro Ser Lys Ser Cys Cys Ser Gly Thr
 50 55 60
 Lys Lys Leu Ser Glu Glu Val Lys Thr Thr Glu Gln Lys Arg Glu Ala
 65 70 75 80
 Cys Lys Cys Ile Val Ala Ala Thr Lys Gly Ile Ser Gly Ile Lys Asn
 85 90 95
 Glu Leu Val Ala Glu Val Pro Lys Lys Cys Gly Ile Thr Thr Thr Leu
 100 105 110
 Pro Pro Ile Thr Ala Asp Phe Asp Cys Ser Lys Ile Glu Ser Thr Ile
 115 120 125
 Phe Arg Gly Tyr Tyr
 130

<210> SEQ ID NO 133

<211> LENGTH: 269

<212> TYPE: PRT

<213> ORGANISM: *Phalaris aquatica* (Canary grass)

<400> SEQUENCE: 133

Met Met Lys Met Val Cys Ser Ser Ser Ser Ser Ser Leu Leu Val Val
 1 5 10 15
 Ala Ala Leu Leu Ala Val Phe Val Gly Ser Ala Gln Gly Ile Ala Lys
 20 25 30
 Val Pro Pro Gly Pro Asn Ile Thr Ala Glu Tyr Gly Asp Lys Trp Leu
 35 40 45
 Asp Ala Lys Ser Thr Trp Tyr Gly Lys Pro Thr Gly Ala Gly Pro Lys
 50 55 60
 Asp Asn Gly Gly Ala Cys Gly Tyr Lys Asp Val Asp Lys Ala Pro Phe
 65 70 75 80
 Asn Gly Met Thr Gly Cys Gly Asn Thr Pro Ile Phe Lys Asp Gly Arg
 85 90 95
 Gly Cys Gly Ser Cys Phe Glu Leu Lys Cys Ser Lys Pro Glu Ser Cys
 100 105 110
 Ser Gly Glu Pro Ile Thr Val His Ile Thr Asp Asp Asn Glu Glu Pro
 115 120 125
 Ile Ala Pro Tyr His Phe Asp Leu Ser Gly His Ala Phe Gly Ser Met
 130 135 140
 Ala Lys Lys Gly Glu Glu Glu Asn Val Arg Gly Ala Gly Glu Leu Glu
 145 150 155 160
 Leu Gln Phe Arg Arg Val Lys Cys Lys Tyr Pro Asp Gly Thr Lys Pro
 165 170 175
 Thr Phe His Val Glu Lys Gly Ser Asn Pro Asn Tyr Leu Ala Leu Leu
 180 185 190
 Val Lys Tyr Val Asp Gly Asp Gly Asp Val Val Ala Val Asp Ile Lys
 195 200 205
 Glu Lys Gly Lys Asp Lys Trp Ile Glu Leu Lys Glu Ser Trp Gly Ala

-continued

```

<210> SEQ ID NO 135
<211> LENGTH: 305
<212> TYPE: PRT
<213> ORGANISM: Phalaris aquatica (Canary grass)

<400> SEQUENCE: 135
Met Ala Val Gln Lys Tyr Thr Val Ala Leu Phe Leu Ala Val Ala Leu
 1           5           10          15
Val Ala Gly Pro Ala Ala Leu Tyr Ala Gly Asp Gly Tyr Ala Pro Ala
 20          25          30
Thr Pro Ala Ala Ser Ala Thr Leu Ala Thr Pro Ala Thr Pro Ala Ala
 35          40          45
Ser Pro Gln His Ala Gly Thr Thr Glu Tyr His Ile Val Arg Lys Ala
 50          55          60
Gly Leu Asn Glu Glu Lys Asn Ala Ala Arg Gln Thr Asp Asp Glu Gln
 65          70          75          80
Lys Arg Ser Asp Glu Ile Asn Cys Pro Asp Phe Asn Lys Ser Val His
 85          90          95
Cys Arg Ala Asp Arg Leu Pro Val Cys Ser Ser Thr Ser Ala His Ser
100         105         110
Ser Lys Gln Asp Val Ala Trp Met Leu Gly Tyr Gly Ser Ile Gln Gly
115         120         125
Phe Ser Met Asp Asp Ala Ser Val Gly Ser Val Ser Ser Glu Phe His
130         135         140
Val Ile Glu Ser Ala Ile Glu Val Ile Thr Tyr Ile Gly Glu Glu Val
145         150         155         160
Lys Val Ile Pro Ala Gly Glu Val Glu Val Ile Asn Lys Val Lys Ala
165         170         175
Ala Phe Ser Thr Ala Ala Thr Ala Ala Asp Glu Ala Pro Ala Asn Asp
180         185         190
Lys Phe Thr Val Phe Val Ser Ser Phe Asn Lys Ala Ile Lys Glu Thr
195         200         205
Thr Gly Gly Ala Tyr Ala Gly Tyr Lys Phe Ile Pro Thr Leu Glu Ala
210         215         220
Ala Val Lys Gln Ala Tyr Ala Ala Ser Ser Ala Thr Ala Pro Glu Val
225         230         235         240
Lys Tyr Ala Val Phe Glu Thr Ala Leu Lys Lys Ala Ile Ser Ala Met
245         250         255
Ser Glu Ala Gln Lys Glu Ala Lys Pro Ala Ala Ala Ile Ser Ala Ala
260         265         270
Thr Thr Thr Ile Ser Ala Ser Thr Ala Thr Pro Ala Ala Pro Pro Pro
275         280         285
Pro Gln Leu Gly Thr Ala Thr Pro Ala Ala Val Ala Gly Gly Tyr Lys
290         295         300

Val
305

```

```

<210> SEQ ID NO 136
<211> LENGTH: 294
<212> TYPE: PRT
<213> ORGANISM: Phalaris aquatica (Canary grass)

<400> SEQUENCE: 136
Met Ala Val Gln Lys Tyr Thr Val Ala Leu Phe Leu Ala Met Ala Leu
 1           5           10          15

```

-continued

Val Ala Gly Pro Ala Ala Ser Tyr Ala Ala Asp Ala Gly Thr Pro Pro
 20 25 30
 Thr Pro Ala Thr Pro Ala Val Pro Gly Ala Ala Ala Gly Lys Ala Thr
 35 40 45
 Thr His Glu Gln Lys Leu Ile Glu Asp Ile Asn Ala Ala Phe Lys Trp
 50 55 60
 Trp Pro Ala Ser Ala Pro Pro Ala Asp Lys Tyr Lys Thr Phe Glu Thr
 65 70 75 80
 Ala Phe Ser Lys Ala Asn Ile Ala Gly Ala Ser Thr Lys Gly Leu Asp
 85 90 95
 Ala Ala Tyr Ser Val Val Tyr Asn Thr Ala Ala Gly Ala Thr Pro Glu
 100 105 110
 Ala Lys Tyr Asp Ser Phe Val Thr Ala Leu Thr Glu Ala Leu Arg Ile
 115 120 125
 Met Ala Gly Thr Leu Glu Val His Ala Val Lys Pro Ala Thr Glu Glu
 130 135 140
 Glu Val Pro Ser Ala Lys Ile Leu Arg Ala Asn Ser Arg Ser Ser Thr
 145 150 155 160
 Arg Ser Ser Arg Phe Lys Ile Ala Ala Thr Val Ala Thr Pro Leu Ser
 165 170 175
 His Ser Thr Ala Ala Asn Ser Ala Pro Ala Asn Asp Lys Phe Thr Val
 180 185 190
 Phe Glu Gly Ala Phe Asn Lys Ala Ile Lys Glu Arg His Gly Gly Pro
 195 200 205
 Thr Glu Thr Tyr Lys Phe Ile Pro Ser Leu Glu Ala Ala Val Lys Gln
 210 215 220
 Ala Tyr Gly Ala Thr Val Ala Arg Ala Pro Glu Val Lys Tyr Ala Val
 225 230 235 240
 Phe Glu Ala Gly Leu Thr Lys Ala Ile Thr Ala Met Ser Glu Ala Gln
 245 250 255
 Lys Val Ala Lys Pro Val Arg Leu Ser Pro Gln Pro Pro Gln Val Leu
 260 265 270
 Pro Leu Ala Ala Gly Gly Ala Ala Thr Val Ala Ala Ala Ser Asp Ser
 275 280 285
 Arg Gly Gly Tyr Lys Val
 290

<210> SEQ ID NO 137

<211> LENGTH: 175

<212> TYPE: PRT

<213> ORGANISM: Phalaris aquatica (Canary grass)

<400> SEQUENCE: 137

Ala Lys Tyr Asp Ala Phe Ile Ala Ala Leu Thr Glu Ala Leu Arg Val
 1 5 10 15
 Ile Ala Gly Ala Phe Glu Val His Ala Val Lys Pro Ala Thr Glu Glu
 20 25 30
 Val Pro Ala Ala Lys Ile Pro Ala Gly Glu Leu Gln Ile Val Asp Lys
 35 40 45
 Ile Asp Ala Ala Phe Lys Ile Ala Ala Thr Ala Ala Asn Ser Ala Pro
 50 55 60
 Ala Asn Asp Lys Phe Thr Val Phe Glu Gly Ala Phe Asn Lys Ala Ile
 65 70 75 80
 Lys Glu Arg His Gly Gly Ala Tyr Glu Thr Tyr Lys Phe Ile Pro Ser
 85 90 95

-continued

Leu Glu Ala Ser Arg Ser Lys Gln Ala Tyr Gly Ala Thr Val Ala Arg
 100 105 110

Ala Pro Glu Val Lys Tyr Ala Val Phe Glu Ala Gly Leu Thr Lys Ala
 115 120 125

Ile Thr Ala Met Ser Glu Ala Gln Lys Val Ala Lys Pro Val Arg Ser
 130 135 140

Val Thr Ala Ala Ala Ala Gly Ala Ala Thr Ala Ala Gly Gly Ala Ala
 145 150 155 160

Thr Val Ala Ala Ser Arg Pro Thr Ser Ala Gly Gly Tyr Lys Val
 165 170 175

<210> SEQ ID NO 138
 <211> LENGTH: 263
 <212> TYPE: PRT
 <213> ORGANISM: Phleum pratense (Common timothy)

<400> SEQUENCE: 138

Met Ala Ser Ser Ser Ser Val Leu Leu Val Val Val Leu Phe Ala Val
 1 5 10 15

Phe Leu Gly Ser Ala Tyr Gly Ile Pro Lys Val Pro Pro Gly Pro Asn
 20 25 30

Ile Thr Ala Thr Tyr Gly Asp Lys Trp Leu Asp Ala Lys Ser Thr Trp
 35 40 45

Tyr Gly Lys Pro Thr Gly Ala Gly Pro Lys Asp Asn Gly Gly Ala Cys
 50 55 60

Gly Tyr Lys Asp Val Asp Lys Pro Pro Phe Ser Gly Met Thr Gly Cys
 65 70 75 80

Gly Asn Thr Pro Ile Phe Lys Ser Gly Arg Gly Cys Gly Ser Cys Phe
 85 90 95

Glu Ile Lys Cys Thr Lys Pro Glu Ala Cys Ser Gly Glu Pro Val Val
 100 105 110

Val His Ile Thr Asp Asp Asn Glu Glu Pro Ile Ala Pro Tyr His Phe
 115 120 125

Asp Leu Ser Gly His Ala Phe Gly Ala Met Ala Lys Lys Gly Asp Glu
 130 135 140

Gln Lys Leu Arg Ser Ala Gly Glu Leu Glu Leu Gln Phe Arg Arg Val
 145 150 155 160

Lys Cys Lys Tyr Pro Glu Gly Thr Lys Val Thr Phe His Val Glu Lys
 165 170 175

Gly Ser Asn Pro Asn Tyr Leu Ala Leu Leu Val Lys Tyr Val Asn Gly
 180 185 190

Asp Gly Asp Val Val Ala Val Asp Ile Lys Glu Lys Gly Lys Asp Lys
 195 200 205

Trp Ile Glu Leu Lys Glu Ser Trp Gly Ala Ile Trp Arg Ile Asp Thr
 210 215 220

Pro Asp Lys Leu Thr Gly Pro Phe Thr Val Arg Tyr Thr Thr Glu Gly
 225 230 235 240

Gly Thr Lys Thr Glu Ala Glu Asp Val Ile Pro Glu Gly Trp Lys Ala
 245 250 255

Asp Thr Ser Tyr Glu Ser Lys
 260

<210> SEQ ID NO 139
 <211> LENGTH: 122
 <212> TYPE: PRT

-continued

<213> ORGANISM: Phleum pratense (Common timothy)

<400> SEQUENCE: 139

Met Ser Met Ala Ser Ser Ser Ser Ser Ser Leu Leu Ala Met Ala Val
 1 5 10 15
 Leu Ala Ala Leu Phe Ala Gly Ala Trp Cys Val Pro Lys Val Thr Phe
 20 25 30
 Thr Val Glu Lys Gly Ser Asn Glu Lys His Leu Ala Val Leu Val Lys
 35 40 45
 Tyr Glu Gly Asp Thr Met Ala Glu Val Glu Leu Arg Glu His Gly Ser
 50 55 60
 Asp Glu Trp Val Ala Met Thr Lys Gly Glu Gly Gly Val Trp Thr Phe
 65 70 75 80
 Asp Ser Glu Glu Pro Leu Gln Gly Pro Phe Asn Phe Arg Phe Leu Thr
 85 90 95
 Glu Lys Gly Met Lys Asn Val Phe Asp Asp Val Val Pro Glu Lys Tyr
 100 105 110
 Thr Ile Gly Ala Thr Tyr Ala Pro Glu Glu
 115 120

<210> SEQ ID NO 140

<211> LENGTH: 286

<212> TYPE: PRT

<213> ORGANISM: Phleum pratense (Common timothy)

<400> SEQUENCE: 140

Ala Asp Leu Gly Tyr Gly Pro Ala Thr Pro Ala Ala Pro Ala Ala Gly
 1 5 10 15
 Tyr Thr Pro Ala Thr Pro Ala Ala Pro Ala Gly Ala Asp Ala Ala Gly
 20 25 30
 Lys Ala Thr Thr Glu Glu Gln Lys Leu Ile Glu Lys Ile Asn Ala Gly
 35 40 45
 Phe Lys Ala Ala Leu Ala Gly Ala Gly Val Gln Pro Ala Asp Lys Tyr
 50 55 60
 Arg Thr Phe Val Ala Thr Phe Gly Pro Ala Ser Asn Lys Ala Phe Ala
 65 70 75 80
 Glu Gly Leu Ser Gly Glu Pro Lys Gly Ala Ala Glu Ser Ser Ser Lys
 85 90 95
 Ala Ala Leu Thr Ser Lys Leu Asp Ala Ala Tyr Lys Leu Ala Tyr Lys
 100 105 110
 Thr Ala Glu Gly Ala Thr Pro Glu Ala Lys Tyr Asp Ala Tyr Val Ala
 115 120 125
 Thr Leu Ser Glu Ala Leu Arg Ile Ile Ala Gly Thr Leu Glu Val His
 130 135 140
 Ala Val Lys Pro Ala Ala Glu Glu Val Lys Val Ile Pro Ala Gly Glu
 145 150 155 160
 Leu Gln Val Ile Glu Lys Val Asp Ala Ala Phe Lys Val Ala Ala Thr
 165 170 175
 Ala Ala Asn Ala Ala Pro Ala Asn Asp Lys Phe Thr Val Phe Glu Ala
 180 185 190
 Ala Phe Asn Asp Glu Ile Lys Ala Ser Thr Gly Gly Ala Tyr Glu Ser
 195 200 205
 Tyr Lys Phe Ile Pro Ala Leu Glu Ala Ala Val Lys Gln Ala Tyr Ala
 210 215 220
 Ala Thr Val Ala Thr Ala Pro Glu Val Lys Tyr Thr Val Phe Glu Thr

-continued

225	230	235	240
Ala Leu Lys Lys Ala Ile Thr Ala Met Ser Glu Ala Gln Lys Ala Ala	245	250	255
Lys Pro Ala Ala Ala Ala Thr Ala Thr Ala Thr Ala Ala Val Gly Ala	260	265	270
Ala Thr Gly Ala Ala Thr Ala Ala Thr Gly Gly Tyr Lys Val	275	280	285

<210> SEQ ID NO 141
 <211> LENGTH: 284
 <212> TYPE: PRT
 <213> ORGANISM: Phleum pratense (Common timothy)

<400> SEQUENCE: 141

Ala Ala Ala Ala Val Pro Arg Arg Gly Pro Arg Gly Gly Pro Gly Arg	1	5	10	15
Ser Tyr Thr Ala Asp Ala Gly Tyr Ala Pro Ala Thr Pro Ala Ala Ala	20	25	30	
Gly Ala Ala Ala Gly Lys Ala Thr Thr Glu Glu Gln Lys Leu Ile Glu	35	40	45	
Asp Ile Asn Val Gly Phe Lys Ala Ala Val Ala Ala Ala Ala Ser Val	50	55	60	
Pro Ala Ala Asp Lys Phe Lys Thr Phe Glu Ala Ala Phe Thr Ser Ser	65	70	75	80
Ser Lys Ala Ala Ala Ala Lys Ala Pro Gly Leu Val Pro Lys Leu Asp	85	90	95	
Ala Ala Tyr Ser Val Ala Tyr Lys Ala Ala Val Gly Ala Thr Pro Glu	100	105	110	
Ala Lys Phe Asp Ser Phe Val Ala Ser Leu Thr Glu Ala Leu Arg Val	115	120	125	
Ile Ala Gly Ala Leu Glu Val His Ala Val Lys Pro Val Thr Glu Glu	130	135	140	
Pro Gly Met Ala Lys Ile Pro Ala Gly Glu Leu Gln Ile Ile Asp Lys	145	150	155	160
Ile Asp Ala Ala Phe Lys Val Ala Ala Thr Ala Ala Ala Thr Ala Pro	165	170	175	
Ala Asp Asp Lys Phe Thr Val Phe Glu Ala Ala Phe Asn Lys Ala Ile	180	185	190	
Lys Glu Ser Thr Gly Gly Ala Tyr Asp Thr Tyr Lys Cys Ile Pro Ser	195	200	205	
Leu Glu Ala Ala Val Lys Gln Ala Tyr Ala Ala Thr Val Ala Ala Ala	210	215	220	
Pro Gln Val Lys Tyr Ala Val Phe Glu Ala Ala Leu Thr Lys Ala Ile	225	230	235	240
Thr Ala Met Ser Glu Val Gln Lys Val Ser Gln Pro Ala Thr Gly Ala	245	250	255	
Ala Thr Val Ala Ala Gly Ala Ala Thr Thr Ala Ala Gly Ala Ala Ser	260	265	270	
Gly Ala Ala Thr Val Ala Ala Gly Gly Tyr Lys Val	275	280		

<210> SEQ ID NO 142
 <211> LENGTH: 132
 <212> TYPE: PRT
 <213> ORGANISM: Phleum pratense (Common timothy)

-continued

<400> SEQUENCE: 142

```

Met Val Ala Met Phe Leu Ala Val Ala Val Val Leu Gly Leu Ala Thr
 1           5           10           15

Ser Pro Thr Ala Glu Gly Gly Lys Ala Thr Thr Glu Glu Gln Lys Leu
          20           25           30

Ile Glu Asp Val Asn Ala Ser Phe Arg Ala Ala Met Ala Thr Thr Ala
          35           40           45

Asn Val Pro Pro Ala Asp Lys Tyr Lys Thr Phe Glu Ala Ala Phe Thr
 50           55           60

Val Ser Ser Lys Arg Asn Leu Ala Asp Ala Val Ser Lys Ala Pro Gln
 65           70           75           80

Leu Val Pro Lys Leu Asp Glu Val Tyr Asn Ala Ala Tyr Asn Ala Ala
          85           90           95

Asp His Ala Ala Pro Glu Asp Lys Tyr Glu Ala Phe Val Leu His Phe
          100           105           110

Ser Glu Ala Leu Arg Ile Ile Ala Gly Thr Pro Glu Val His Ala Val
 115           120           125

Lys Pro Gly Ala
 130

```

<210> SEQ ID NO 143

<211> LENGTH: 131

<212> TYPE: PRT

<213> ORGANISM: Phleum pratense (Common timothy)

<400> SEQUENCE: 143

```

Met Ser Trp Gln Thr Tyr Val Asp Glu His Leu Met Cys Glu Ile Glu
 1           5           10           15

Gly His His Leu Ala Ser Ala Ala Ile Leu Gly His Asp Gly Thr Val
          20           25           30

Trp Ala Gln Ser Ala Asp Phe Pro Gln Phe Lys Pro Glu Glu Ile Thr
 35           40           45

Gly Ile Met Lys Asp Phe Asp Glu Pro Gly His Leu Ala Pro Thr Gly
 50           55           60

Met Phe Val Ala Gly Ala Lys Tyr Met Val Ile Gln Gly Glu Pro Gly
 65           70           75           80

Arg Val Ile Arg Gly Lys Lys Gly Ala Gly Gly Ile Thr Ile Lys Lys
          85           90           95

Thr Gly Gln Ala Leu Val Val Gly Ile Tyr Asp Glu Pro Met Thr Pro
          100           105           110

Gly Gln Cys Asn Met Val Val Glu Arg Leu Gly Asp Tyr Leu Val Glu
 115           120           125

Gln Gly Met
 130

```

<210> SEQ ID NO 144

<211> LENGTH: 131

<212> TYPE: PRT

<213> ORGANISM: Phleum pratense (Common timothy)

<400> SEQUENCE: 144

```

Met Ser Trp Gln Thr Tyr Val Asp Glu His Leu Met Cys Glu Ile Glu
 1           5           10           15

Gly His His Leu Ala Ser Ala Ala Ile Leu Gly His Asp Gly Thr Val
          20           25           30

Trp Ala Gln Ser Ala Asp Phe Pro Gln Phe Lys Pro Glu Glu Ile Thr

```


-continued

85				90				95							
Phe	Pro	Ala	Lys	Pro	Ala	Pro	Lys	Val	Ala	Ala	Tyr	Thr	Pro	Ala	Ala
			100												110
Pro	Ala	Gly	Ala	Ala	Pro	Lys	Ala	Thr	Thr	Asp	Glu	Gln	Lys	Leu	Ile
			115												125
Glu	Lys	Ile	Asn	Val	Gly	Phe	Lys	Ala	Ala	Val	Ala	Ala	Ala	Ala	Gly
			130												140
Val	Pro	Ala	Ala	Ser	Lys	Tyr	Lys	Thr	Phe	Val	Ala	Thr	Phe	Gly	Ala
															160
Ala	Ser	Asn	Lys	Ala	Phe	Ala	Glu	Ala	Leu	Ser	Thr	Glu	Pro	Lys	Gly
															175
Ala	Ala	Val	Ala	Ser	Ser	Lys	Ala	Val	Leu	Thr	Ser	Lys	Leu	Asp	Ala
															190
Ala	Tyr	Lys	Leu	Ala	Tyr	Lys	Ser	Ala	Glu	Gly	Ala	Thr	Pro	Glu	Ala
															205
Lys	Tyr	Asp	Ala	Tyr	Val	Ala	Thr	Leu	Ser	Glu	Ala	Leu	Arg	Ile	Ile
															220
Ala	Gly	Thr	Leu	Glu	Val	His	Gly	Val	Lys	Pro	Ala	Ala	Glu	Glu	Val
															240
Lys	Ala	Ile	Pro	Ala	Gly	Glu	Leu	Gln	Val	Ile	Asp	Lys	Val	Asp	Ala
															255
Ala	Phe	Lys	Val	Ala	Ala	Thr	Ala	Ala	Asn	Ala	Ala	Pro	Ala	Asn	Asp
															270
Lys	Phe	Thr	Val	Phe	Glu	Ala	Ala	Phe	Asn	Asp	Ala	Ile	Lys	Ala	Ser
															285
Thr	Gly	Gly	Ala	Tyr	Gln	Ser	Tyr	Lys	Phe	Ile	Pro	Ala	Leu	Glu	Ala
															300
Ala	Val	Lys	Gln	Ser	Tyr	Ala	Ala	Thr	Val	Ala	Thr	Ala	Pro	Ala	Val
															320
Lys	Tyr	Thr	Val	Phe	Glu	Thr	Ala	Leu	Lys	Lys	Ala	Ile	Thr	Ala	Met
															335
Ser	Gln	Ala	Gln	Lys	Ala	Ala	Lys	Pro	Ala	Ala	Ala	Val	Thr	Gly	Thr
															350
Ala	Thr	Ser	Ala	Val	Gly	Ala	Ala	Thr	Gly	Ala	Ala	Thr	Ala	Ala	Ala
															365
Gly	Gly	Tyr	Lys	Val											
															370

<210> SEQ ID NO 147

<211> LENGTH: 333

<212> TYPE: PRT

<213> ORGANISM: Poa pratensis (Kentucky bluegrass)

<400> SEQUENCE: 147

Met	Ala	Val	His	Gln	Tyr	Thr	Val	Ala	Leu	Phe	Leu	Ala	Val	Ala	Leu
															15
Val	Ala	Gly	Pro	Ala	Ala	Ser	Tyr	Ala	Ala	Asp	Val	Gly	Tyr	Gly	Ala
															30
Pro	Ala	Thr	Leu	Ala	Thr	Pro	Ala	Thr	Pro	Ala	Ala	Pro	Ala	Ala	Gly
															45
Tyr	Thr	Pro	Ala	Ala	Pro	Ala	Gly	Ala	Ala	Pro	Lys	Ala	Thr	Thr	Asp
															60
Glu	Gln	Lys	Leu	Ile	Glu	Lys	Ile	Asn	Ala	Gly	Phe	Lys	Ala	Ala	Val
															80

-continued

Ala Ala Ala Ala Gly Val Pro Ala Val Asp Lys Tyr Lys Thr Phe Val
85 90 95

Ala Thr Phe Gly Thr Ala Ser Asn Lys Ala Phe Ala Glu Ala Leu Ser
100 105 110

Thr Glu Pro Lys Gly Ala Ala Ala Ala Ser Ser Asn Ala Val Leu Thr
115 120 125

Ser Lys Leu Asp Ala Ala Tyr Lys Leu Ala Tyr Lys Ser Ala Glu Gly
130 135 140

Ala Thr Pro Glu Ala Lys Tyr Asp Ala Tyr Val Ala Thr Leu Ser Glu
145 150 155 160

Ala Leu Arg Ile Ile Ala Gly Thr Leu Glu Val His Ala Val Lys Pro
165 170 175

Ala Gly Glu Glu Val Lys Ala Ile Pro Ala Gly Glu Leu Gln Val Ile
180 185 190

Asp Lys Val Asp Ala Ala Phe Lys Val Ala Ala Thr Ala Ala Asn Ala
195 200 205

Ala Pro Ala Asn Asp Lys Phe Thr Val Phe Glu Ala Ala Phe Asn Asp
210 215 220

Ala Ile Lys Ala Ser Thr Gly Gly Ala Tyr Gln Ser Tyr Lys Phe Ile
225 230 235 240

Pro Ala Leu Glu Ala Ala Val Lys Gln Ser Tyr Ala Ala Thr Val Ala
245 250 255

Thr Ala Pro Ala Val Lys Tyr Thr Val Phe Glu Thr Ala Leu Lys Lys
260 265 270

Ala Ile Thr Ala Met Ser Gln Ala Gln Lys Ala Ala Lys Pro Ala Ala
275 280 285

Ala Val Thr Ala Thr Ala Thr Gly Ala Val Gly Ala Ala Thr Gly Ala
290 295 300

Val Gly Ala Ala Thr Gly Ala Ala Thr Ala Ala Ala Gly Gly Tyr Lys
305 310 315 320

Thr Gly Ala Ala Thr Pro Thr Ala Gly Gly Tyr Lys Val
325 330

<210> SEQ ID NO 148

<211> LENGTH: 307

<212> TYPE: PRT

<213> ORGANISM: *Poa pratensis* (Kentucky bluegrass)

<400> SEQUENCE: 148

Met Ala Val Gln Lys Tyr Thr Val Ala Leu Phe Leu Val Ala Leu Val
1 5 10 15

Val Gly Pro Ala Ala Ser Tyr Ala Ala Asp Leu Ser Tyr Gly Ala Pro
20 25 30

Ala Thr Pro Ala Ala Pro Ala Ala Gly Tyr Thr Pro Ala Ala Pro Ala
35 40 45

Gly Ala Ala Pro Lys Ala Thr Thr Asp Glu Gln Lys Met Ile Glu Lys
50 55 60

Ile Asn Val Gly Phe Lys Ala Ala Val Ala Ala Ala Gly Gly Val Pro
65 70 75 80

Ala Ala Asn Lys Tyr Lys Thr Phe Val Ala Thr Phe Gly Ala Ala Ser
85 90 95

Asn Lys Ala Phe Ala Glu Ala Leu Ser Thr Glu Pro Lys Gly Ala Ala
100 105 110

Val Asp Ser Ser Lys Ala Ala Leu Thr Ser Lys Leu Asp Ala Ala Tyr
115 120 125

-continued

Lys Leu Ala Tyr Lys Ser Ala Glu Gly Ala Thr Pro Glu Ala Lys Tyr
 130 135 140
 Asp Asp Tyr Val Ala Thr Leu Ser Glu Ala Leu Arg Ile Ile Ala Gly
 145 150 155 160
 Thr Leu Glu Val His Gly Val Lys Pro Ala Ala Glu Glu Val Lys Ala
 165 170 175
 Thr Pro Ala Gly Glu Leu Gln Val Ile Asp Lys Val Asp Ala Ala Phe
 180 185 190
 Lys Val Ala Ala Thr Ala Ala Asn Ala Ala Pro Ala Asn Asp Lys Phe
 195 200 205
 Thr Val Phe Glu Ala Ala Phe Asn Asp Ala Ile Lys Ala Ser Thr Gly
 210 215 220
 Gly Ala Tyr Gln Ser Tyr Lys Phe Ile Pro Ala Leu Glu Ala Ala Val
 225 230 235 240
 Lys Gln Ser Tyr Ala Ala Thr Val Ala Thr Ala Pro Ala Val Lys Tyr
 245 250 255
 Thr Val Phe Glu Thr Ala Leu Lys Lys Ala Ile Thr Ala Met Ser Gln
 260 265 270
 Ala Gln Lys Ala Ala Lys Pro Ala Ala Ala Thr Gly Thr Ala Thr
 275 280 285
 Ala Ala Val Gly Ala Ala Thr Gly Ala Ala Thr Ala Ala Ala Gly Gly
 290 295 300
 Tyr Lys Val
 305

<210> SEQ ID NO 149
 <211> LENGTH: 209
 <212> TYPE: PRT
 <213> ORGANISM: Polistes annularis (Paper wasp)

<400> SEQUENCE: 149

Ser Ser Gln Gly Val Asp Tyr Cys Lys Ile Lys Cys Pro Ser Gly Ile
 1 5 10 15
 His Thr Val Cys Gln Tyr Gly Glu Ser Thr Lys Pro Ser Lys Asn Cys
 20 25 30
 Ala Gly Lys Val Ile Lys Ser Val Gly Pro Thr Glu Glu Glu Lys Lys
 35 40 45
 Leu Ile Val Ser Glu His Asn Arg Phe Arg Gln Lys Val Ala Gln Gly
 50 55 60
 Leu Glu Thr Arg Gly Asn Pro Gly Pro Gln Pro Ala Ala Ser Asp Met
 65 70 75 80
 Asn Asp Leu Val Trp Asn Asp Glu Leu Ala His Ile Ala Gln Val Trp
 85 90 95
 Ala Ser Gln Cys Gln Phe Leu Val His Asp Lys Cys Arg Asn Thr Ala
 100 105 110
 Lys Tyr Pro Val Gly Gln Asn Ile Ala Tyr Ala Gly Gly Ser Asn Leu
 115 120 125
 Pro Asp Val Val Ser Leu Ile Lys Leu Trp Glu Asn Glu Val Lys Asp
 130 135 140
 Phe Asn Tyr Asn Thr Gly Ile Thr Lys Gln Asn Phe Ala Lys Ile Gly
 145 150 155 160
 His Tyr Thr Gln Met Val Trp Gly Lys Thr Lys Glu Ile Gly Cys Gly
 165 170 175
 Ser Leu Lys Tyr Met Glu Asn Asn Met Gln Asn His Tyr Leu Ile Cys

-continued

180	185	190
Asn Tyr Gly Pro Ala Gly Asn Tyr Leu Gly Gln Leu Pro Tyr Thr Lys 195	200	205
Lys		
<210> SEQ ID NO 150		
<211> LENGTH: 206		
<212> TYPE: PRT		
<213> ORGANISM: Polistes dominulus (European paper wasp)		
<400> SEQUENCE: 150		
Asn Asp Tyr Cys Lys Ile Lys Cys Ser Ser Gly Val His Thr Val Cys 1	5	10 15
Gln Tyr Gly Glu Ser Thr Lys Pro Ser Lys Asn Cys Ala Gly Lys Leu 20	25	30
Ile Lys Ser Val Gly Pro Thr Glu Glu Glu Lys Lys Leu Ile Val Glu 35	40	45
Glu His Asn Arg Phe Arg Gln Lys Val Ala Lys Gly Leu Glu Thr Arg 50	55	60
Gly Asn Pro Gly Pro Gln Pro Ala Ala Ser Asn Met Asn Asn Leu Val 65	70	75 80
Trp Asn Asp Glu Leu Ala Lys Ile Ala Gln Val Trp Ala Ser Gln Cys 85	90	95
Gln Ile Leu Val His Asp Lys Cys Arg Asn Thr Glu Lys Tyr Gln Val 100	105	110
Gly Gln Asn Ile Ala Tyr Ala Gly Ser Ser Asn His Phe Pro Ser Val 115	120	125
Thr Lys Leu Ile Gln Leu Trp Glu Asn Glu Val Lys Asp Phe Asn Tyr 130	135	140
Asn Thr Gly Ile Thr Asn Lys Asn Phe Gly Lys Val Gly His Tyr Thr 145	150	155 160
Gln Met Val Trp Gly Asn Thr Lys Glu Val Gly Cys Gly Ser Leu Lys 165	170	175
Tyr Val Glu Lys Asn Met Gln Ile His Tyr Leu Ile Cys Asn Tyr Gly 180	185	190
Pro Ala Gly Asn Tyr Leu Gly Gln Pro Ile Tyr Thr Lys Lys 195	200	205

<210> SEQ ID NO 151		
<211> LENGTH: 205		
<212> TYPE: PRT		
<213> ORGANISM: Polistes exclamans (Paper wasp)		
<400> SEQUENCE: 151		
Val Asp Tyr Cys Lys Ile Lys Cys Pro Ser Gly Ile His Thr Val Cys 1	5	10 15
Gln Tyr Gly Glu Ser Thr Lys Pro Ser Lys Asn Cys Ala Gly Lys Val 20	25	30
Ile Lys Ser Val Gly Pro Thr Glu Glu Glu Lys Lys Leu Ile Val Ser 35	40	45
Glu His Asn Arg Phe Arg Gln Lys Val Ala Gln Gly Leu Glu Thr Arg 50	55	60
Gly Asn Pro Gly Pro Gln Pro Ala Ala Ser Asp Met Asn Asp Leu Val 65	70	75 80
Trp Asn Asp Glu Leu Ala His Ile Ala Gln Val Trp Ala Ser Gln Cys 85	90	95

-continued

Gln Phe Leu Val His Asp Lys Cys Arg Asn Thr Ala Lys Tyr Pro Val
 100 105 110

Gly Gln Asn Ile Ala Tyr Ala Gly Gly Ser Lys Leu Pro Asp Val Val
 115 120 125

Ser Leu Ile Lys Leu Trp Glu Asn Glu Val Lys Asp Phe Asn Tyr Asn
 130 135 140

Thr Gly Ile Thr Lys Gln Asn Phe Ala Lys Ile Gly His Tyr Thr Gln
 145 150 155 160

Met Val Trp Gly Lys Thr Lys Glu Ile Gly Cys Gly Ser Leu Lys Tyr
 165 170 175

Ile Glu Asn Lys Met Gln Asn His Tyr Leu Ile Cys Asn Tyr Gly Pro
 180 185 190

Ala Gly Asn Tyr Leu Gly Gln Leu Pro Tyr Thr Lys Lys
 195 200 205

<210> SEQ ID NO 152
 <211> LENGTH: 205
 <212> TYPE: PRT
 <213> ORGANISM: Polistes fuscatus (Paper wasp)

<400> SEQUENCE: 152

Val Asp Tyr Cys Lys Ile Lys Cys Ser Ser Gly Ile His Thr Val Cys
 1 5 10 15

Gln Tyr Gly Glu Ser Thr Lys Pro Ser Lys Asn Cys Ala Asp Lys Val
 20 25 30

Ile Lys Ser Val Gly Pro Thr Glu Glu Glu Lys Lys Leu Ile Val Asn
 35 40 45

Glu His Asn Arg Phe Arg Gln Lys Val Ala Gln Gly Leu Glu Thr Arg
 50 55 60

Gly Asn Pro Gly Pro Gln Pro Ala Ala Ser Asp Met Asn Asn Leu Val
 65 70 75 80

Trp Asn Asp Glu Leu Ala His Ile Ala Gln Val Trp Ala Ser Gln Cys
 85 90 95

Gln Ile Leu Val His Asp Lys Cys Arg Asn Thr Ala Lys Tyr Gln Val
 100 105 110

Gly Gln Asn Ile Ala Tyr Ala Gly Gly Ser Lys Leu Pro Asp Val Val
 115 120 125

Ser Leu Ile Lys Leu Trp Glu Asn Glu Val Lys Asp Phe Asn Tyr Asn
 130 135 140

Lys Gly Ile Thr Lys Gln Asn Phe Gly Lys Val Gly His Tyr Thr Gln
 145 150 155 160

Met Ile Trp Ala Lys Thr Lys Glu Ile Gly Cys Gly Ser Leu Lys Tyr
 165 170 175

Met Lys Asn Asn Met Gln His His Tyr Leu Ile Cys Asn Tyr Gly Pro
 180 185 190

Ala Gly Asn Tyr Leu Gly Gln Leu Pro Tyr Thr Lys Lys
 195 200 205

<210> SEQ ID NO 153
 <211> LENGTH: 160
 <212> TYPE: PRT
 <213> ORGANISM: Prunus avium (Cherry)

<400> SEQUENCE: 153

Met Gly Val Phe Thr Tyr Glu Ser Glu Phe Thr Ser Glu Ile Pro Pro
 1 5 10 15

-continued

Pro Arg Leu Phe Lys Ala Phe Val Leu Asp Ala Asp Asn Leu Val Pro
 20 25 30

Lys Ile Ala Pro Gln Ala Ile Lys His Ser Glu Ile Leu Glu Gly Asp
 35 40 45

Gly Gly Pro Gly Thr Ile Lys Lys Ile Thr Phe Gly Glu Gly Ser Gln
 50 55 60

Tyr Gly Tyr Val Lys His Lys Ile Asp Ser Ile Asp Lys Glu Asn Tyr
 65 70 75 80

Ser Tyr Ser Tyr Thr Leu Ile Glu Gly Asp Ala Leu Gly Asp Thr Leu
 85 90 95

Glu Lys Ile Ser Tyr Glu Thr Lys Leu Val Ala Ser Pro Ser Gly Gly
 100 105 110

Ser Ile Ile Lys Ser Thr Ser His Tyr His Thr Lys Gly Asn Val Glu
 115 120 125

Ile Lys Glu Glu His Val Lys Ala Gly Lys Glu Lys Ala Ser Asn Leu
 130 135 140

Phe Lys Leu Ile Glu Thr Tyr Leu Lys Gly His Pro Asp Ala Tyr Asn
 145 150 155 160

<210> SEQ ID NO 154
 <211> LENGTH: 181
 <212> TYPE: PRT
 <213> ORGANISM: Rattus norvegicus (Rat)

<400> SEQUENCE: 154

Met Lys Leu Leu Leu Leu Leu Leu Cys Leu Gly Leu Thr Leu Val Cys
 1 5 10 15

Gly His Ala Glu Glu Ala Ser Ser Thr Arg Gly Asn Leu Asp Val Ala
 20 25 30

Lys Leu Asn Gly Asp Trp Phe Ser Ile Val Val Ala Ser Asn Lys Arg
 35 40 45

Glu Lys Ile Glu Glu Asn Gly Ser Met Arg Val Phe Met Gln His Ile
 50 55 60

Asp Val Leu Glu Asn Ser Leu Gly Phe Lys Phe Arg Ile Lys Glu Asn
 65 70 75 80

Gly Glu Cys Arg Glu Leu Tyr Leu Val Ala Tyr Lys Thr Pro Glu Asp
 85 90 95

Gly Glu Tyr Phe Val Glu Tyr Asp Gly Gly Asn Thr Phe Thr Ile Leu
 100 105 110

Lys Thr Asp Tyr Asp Arg Tyr Val Met Phe His Leu Ile Asn Phe Lys
 115 120 125

Asn Gly Glu Thr Phe Gln Leu Met Val Leu Tyr Gly Arg Thr Lys Asp
 130 135 140

Leu Ser Ser Asp Ile Lys Glu Lys Phe Ala Lys Leu Cys Glu Ala His
 145 150 155 160

Gly Ile Thr Arg Asp Asn Ile Ile Asp Leu Thr Lys Thr Asp Arg Cys
 165 170 175

Leu Gln Ala Arg Gly
 180

<210> SEQ ID NO 155
 <211> LENGTH: 138
 <212> TYPE: PRT
 <213> ORGANISM: Solenopsis invicta (Red imported fire ant)

<400> SEQUENCE: 155

-continued

Met Lys Ser Phe Val Leu Ala Thr Cys Leu Leu Gly Phe Ala Gln Ile
 1 5 10 15
 Ile Tyr Ala Asp Asn Lys Glu Leu Lys Ile Ile Arg Lys Asp Val Ala
 20 25 30
 Glu Cys Leu Arg Thr Leu Pro Lys Cys Gly Asn Gln Pro Asp Asp Pro
 35 40 45
 Leu Ala Arg Val Asp Val Trp His Cys Ala Met Ala Lys Arg Gly Val
 50 55 60
 Tyr Asp Asn Pro Asp Pro Ala Val Ile Lys Glu Arg Ser Met Lys Met
 65 70 75 80
 Cys Thr Lys Ile Ile Thr Asp Pro Ala Asn Val Glu Asn Cys Lys Lys
 85 90 95
 Val Ala Ser Arg Cys Val Asp Arg Glu Thr Gln Gly Pro Lys Ser Asn
 100 105 110
 Arg Gln Lys Ala Val Asn Ile Ile Gly Cys Ala Leu Arg Ala Gly Val
 115 120 125
 Ala Glu Thr Thr Val Leu Ala Arg Lys Lys
 130 135

<210> SEQ ID NO 156

<211> LENGTH: 212

<212> TYPE: PRT

<213> ORGANISM: Solenopsis invicta (Red imported fire ant)

<400> SEQUENCE: 156

Thr Asn Tyr Cys Asn Leu Gln Ser Cys Lys Arg Asn Asn Ala Ile His
 1 5 10 15
 Thr Met Cys Gln Tyr Thr Ser Pro Thr Pro Gly Pro Met Cys Leu Glu
 20 25 30
 Tyr Ser Asn Val Gly Phe Thr Asp Ala Glu Lys Asp Ala Ile Val Asn
 35 40 45
 Lys His Asn Glu Leu Arg Gln Arg Val Ala Ser Gly Lys Glu Met Arg
 50 55 60
 Gly Thr Asn Gly Pro Gln Pro Pro Ala Val Lys Met Pro Asn Leu Thr
 65 70 75 80
 Trp Asp Pro Glu Leu Ala Thr Ile Ala Gln Arg Trp Ala Asn Gln Cys
 85 90 95
 Thr Phe Glu His Asp Ala Cys Arg Asn Val Glu Arg Phe Ala Val Gly
 100 105 110
 Gln Asn Ile Ala Ala Thr Ser Ser Ser Gly Lys Asn Lys Ser Thr Pro
 115 120 125
 Asn Glu Met Ile Leu Leu Trp Tyr Asn Glu Val Lys Asp Phe Asp Asn
 130 135 140
 Arg Trp Ile Ser Ser Phe Pro Ser Asp Asp Asn Ile Leu Met Lys Val
 145 150 155 160
 Glu His Tyr Thr Gln Ile Val Trp Ala Lys Thr Ser Lys Ile Gly Cys
 165 170 175
 Ala Arg Ile Met Phe Lys Glu Pro Asp Asn Trp Thr Lys His Tyr Leu
 180 185 190
 Val Cys Asn Tyr Gly Pro Ala Gly Asn Val Leu Gly Ala Pro Ile Tyr
 195 200 205
 Glu Ile Lys Lys
 210

-continued

<210> SEQ ID NO 157
 <211> LENGTH: 117
 <212> TYPE: PRT
 <213> ORGANISM: *Solenopsis invicta* (Red imported fire ant)

 <400> SEQUENCE: 157

 Leu Asp Ile Lys Glu Ile Ser Ile Met Asn Arg Ile Leu Glu Lys Cys
 1 5 10 15
 Ile Arg Thr Val Pro Lys Arg Glu Asn Asp Pro Ile Asn Pro Leu Lys
 20 25 30
 Asn Val Asn Val Leu Tyr Cys Ala Phe Thr Lys Arg Gly Ile Phe Thr
 35 40 45
 Pro Lys Gly Val Asn Thr Lys Gln Tyr Ile Asn Tyr Cys Glu Lys Thr
 50 55 60
 Ile Ile Ser Pro Ala Asp Ile Lys Leu Cys Lys Lys Ile Ala Ser Lys
 65 70 75 80
 Cys Val Lys Lys Val Tyr Asp Arg Pro Gly Pro Val Ile Glu Arg Ser
 85 90 95
 Lys Asn Leu Leu Ser Cys Val Leu Lys Lys Gly Leu Leu Glu Leu Thr
 100 105 110
 Val Tyr Gly Lys Asn
 115

<210> SEQ ID NO 158
 <211> LENGTH: 119
 <212> TYPE: PRT
 <213> ORGANISM: *Solenopsis richteri* (Black imported fire ant)

 <400> SEQUENCE: 158

 Asp Ile Glu Ala Gln Arg Val Leu Arg Lys Asp Ile Ala Glu Cys Ala
 1 5 10 15
 Arg Thr Leu Pro Lys Cys Val Asn Gln Pro Asp Asp Pro Leu Ala Arg
 20 25 30
 Val Asp Val Trp His Cys Ala Met Ser Lys Arg Gly Val Tyr Asp Asn
 35 40 45
 Pro Asp Pro Ala Val Val Lys Glu Lys Asn Ser Lys Met Cys Pro Lys
 50 55 60
 Ile Ile Thr Asp Pro Ala Asp Val Glu Asn Cys Lys Lys Val Val Ser
 65 70 75 80
 Arg Cys Val Asp Arg Glu Thr Gln Arg Pro Arg Ser Asn Arg Gln Lys
 85 90 95
 Ala Ile Asn Ile Thr Gly Cys Ile Leu Arg Ala Gly Val Val Glu Ala
 100 105 110
 Thr Val Leu Ala Arg Glu Lys
 115

<210> SEQ ID NO 159
 <211> LENGTH: 211
 <212> TYPE: PRT
 <213> ORGANISM: *Solenopsis richteri* (Black imported fire ant)

 <400> SEQUENCE: 159

 Thr Asn Tyr Cys Asn Leu Gln Ser Cys Lys Arg Asn Asn Ala Ile His
 1 5 10 15
 Thr Met Cys Gln Tyr Thr Ser Pro Thr Pro Gly Pro Met Cys Leu Glu
 20 25 30
 Tyr Ser Asn Val Gly Phe Thr Asp Ala Glu Lys Asp Ala Ile Val Asn
 35 40 45

-continued

Lys His Asn Glu Leu Arg Gln Arg Val Ala Ser Gly Lys Glu Met Arg
 50 55 60
 Gly Thr Asn Gly Pro Gln Pro Pro Ala Val Lys Met Pro Asn Leu Thr
 65 70 75 80
 Trp Asp Pro Glu Leu Ala Thr Ile Ala Gln Arg Trp Ala Asn Gln Cys
 85 90 95
 Thr Phe Glu His Asp Ala Cys Arg Asn Val Glu Arg Phe Ala Val Gly
 100 105 110
 Gln Asn Ile Ala Ala Thr Ser Ser Ser Gly Lys Asn Lys Ser Thr Leu
 115 120 125
 Ser Asp Met Ile Leu Leu Trp Tyr Asn Glu Val Lys Asp Phe Asp Asn
 130 135 140
 Arg Trp Ile Ser Ser Phe Pro Ser Asp Gly Asn Ile Leu Met His Val
 145 150 155 160
 Gly His Tyr Thr Gln Ile Val Trp Ala Lys Thr Lys Lys Ile Gly Cys
 165 170 175
 Gly Arg Ile Met Phe Lys Glu Asp Asn Trp Asn Lys His Tyr Leu Val
 180 185 190
 Cys Asn Tyr Gly Pro Ala Gly Asn Val Leu Gly Ala Gln Ile Tyr Glu
 195 200 205
 Ile Lys Lys
 210

<210> SEQ ID NO 160
 <211> LENGTH: 202
 <212> TYPE: PRT
 <213> ORGANISM: Vespa crabro (European hornet)

<400> SEQUENCE: 160

Asn Asn Tyr Cys Lys Ile Lys Cys Arg Ser Gly Ile His Thr Leu Cys
 1 5 10 15
 Lys Tyr Gly Thr Ser Thr Lys Pro Asn Cys Gly Lys Asn Val Val Lys
 20 25 30
 Ala Ser Gly Leu Thr Lys Gln Glu Asn Leu Glu Ile Leu Lys Gln His
 35 40 45
 Asn Glu Phe Arg Gln Lys Val Ala Arg Gly Leu Glu Thr Arg Gly Asn
 50 55 60
 Pro Gly Pro Gln Pro Pro Ala Lys Ser Met Asn Thr Leu Val Trp Asn
 65 70 75 80
 Asp Glu Leu Ala Gln Ile Ala Gln Val Trp Ala Asn Gln Cys Asn Tyr
 85 90 95
 Gly His Asp Asn Cys Arg Asn Ser Ala Lys Tyr Ser Val Gly Gln Asn
 100 105 110
 Ile Ala Glu Gly Ser Thr Thr Ala Asp Asn Phe Gly Ser Val Ser Asn
 115 120 125
 Met Val Lys Met Trp Glu Asp Glu Val Lys Asp Tyr Gln Tyr Gly Ser
 130 135 140
 Pro Lys Asn Lys Leu Asn Lys Val Gly His Tyr Thr Gln Met Val Trp
 145 150 155 160
 Ala Lys Thr Lys Glu Ile Gly Cys Gly Ser Ile Lys Tyr Ile Glu Asn
 165 170 175
 Gly Trp His Arg His Tyr Leu Val Cys Asn Tyr Gly Pro Ala Gly Asn
 180 185 190
 Val Gly Asn Glu Pro Ile Tyr Glu Arg Lys

-continued

115	120	125
Leu Val Lys Met Trp Glu Asp Glu Val Lys Asp Tyr Asn Pro Lys Lys 130 135 140		
Lys Phe Ser Gly Asn Asn Phe Leu Lys Thr Gly His Tyr Thr Gln Met 145 150 155 160		
Val Trp Ala Asn Thr Lys Glu Val Gly Cys Gly Ser Ile Lys Phe Ile 165 170 175		
Gln Glu Lys Trp His Lys His Tyr Leu Val Cys Asn Tyr Gly Pro Ser 180 185 190		
Gly Asn Phe Gln Asn Glu Glu Leu Tyr Gln Thr Lys 195 200		

<210> SEQ ID NO 163
 <211> LENGTH: 204
 <212> TYPE: PRT
 <213> ORGANISM: *Vespula germanica* (Yellow jacket) (Wasp)

<400> SEQUENCE: 163

Asn Asn Tyr Cys Lys Ile Lys Cys Leu Lys Gly Gly Val His Thr Ala 1 5 10 15		
Cys Lys Tyr Glu Ser Leu Lys Pro Asn Cys Ala Asn Lys Lys Val Val 20 25 30		
Ala Tyr Gly Leu Thr Lys Gln Glu Lys Gln Asp Ile Leu Lys Glu His 35 40 45		
Asn Asp Phe Arg Gln Lys Ile Ala Arg Gly Leu Glu Thr Arg Gly Asn 50 55 60		
Pro Gly Pro Gln Pro Pro Ala Lys Asn Met Lys Asn Leu Val Trp Ser 65 70 75 80		
Asp Glu Leu Ala Tyr Ile Ala Gln Val Trp Ala Asn Gln Cys Gln Tyr 85 90 95		
Gly His Asp Thr Cys Arg Asp Val Ala Lys Tyr Pro Val Gly Gln Asn 100 105 110		
Val Ala Leu Thr Gly Ser Thr Ala Ala Lys Tyr Asp Asn Pro Val Lys 115 120 125		
Leu Val Lys Met Trp Glu Asp Glu Val Lys Asp Tyr Asn Pro Lys Lys 130 135 140		
Lys Phe Ser Glu Asn Asn Phe Leu Lys Ile Gly His Tyr Thr Gln Met 145 150 155 160		
Val Trp Ala Asn Thr Lys Glu Val Gly Cys Gly Ser Ile Lys Tyr Ile 165 170 175		
Gln Asp Lys Trp His Lys His Tyr Leu Val Cys Asn Tyr Gly Pro Ser 180 185 190		
Gly Asn Phe Gly Asn Glu Glu Leu Tyr Gln Thr Lys 195 200		

<210> SEQ ID NO 164
 <211> LENGTH: 300
 <212> TYPE: PRT
 <213> ORGANISM: *Vespula maculifrons* (Eastern yellow jacket) (Wasp)

<400> SEQUENCE: 164

Gly Pro Lys Cys Pro Phe Asn Ser Asp Thr Val Ser Ile Ile Ile Glu 1 5 10 15		
Thr Arg Glu Asn Arg Asn Arg Asp Leu Tyr Thr Leu Gln Thr Leu Gln 20 25 30		
Asn His Pro Glu Phe Lys Lys Lys Thr Ile Thr Arg Pro Val Val Phe		

-continued

35				40				45							
Ile	Thr	His	Gly	Phe	Thr	Ser	Ser	Ala	Ser	Glu	Lys	Asn	Phe	Ile	Asn
50						55				60					
Leu	Ala	Lys	Ala	Leu	Val	Asp	Lys	Asp	Asn	Tyr	Met	Val	Ile	Ser	Ile
65				70						75				80	
Asp	Trp	Gln	Thr	Ala	Ala	Cys	Thr	Asn	Glu	Tyr	Pro	Gly	Leu	Lys	Tyr
				85					90					95	
Ala	Tyr	Tyr	Pro	Thr	Ala	Ala	Ser	Asn	Thr	Arg	Leu	Val	Gly	Gln	Tyr
			100					105					110		
Ile	Ala	Thr	Ile	Thr	Gln	Lys	Leu	Val	Lys	Asp	Tyr	Lys	Ile	Ser	Met
		115					120					125			
Ala	Asn	Ile	Arg	Leu	Ile	Gly	His	Ser	Leu	Gly	Ala	His	Val	Ser	Gly
	130					135					140				
Phe	Ala	Gly	Lys	Arg	Val	Gln	Glu	Leu	Lys	Leu	Gly	Lys	Tyr	Ser	Glu
145					150					155					160
Ile	Ile	Gly	Leu	Asp	Pro	Ala	Arg	Pro	Ser	Phe	Asp	Ser	Asn	His	Cys
				165					170					175	
Ser	Glu	Arg	Leu	Cys	Glu	Thr	Asp	Ala	Glu	Tyr	Val	Gln	Ile	Ile	His
			180					185					190		
Thr	Ser	Asn	Tyr	Leu	Gly	Thr	Glu	Lys	Ile	Leu	Gly	Thr	Val	Asp	Phe
		195					200					205			
Tyr	Met	Asn	Asn	Gly	Lys	Asn	Asn	Pro	Gly	Cys	Gly	Arg	Phe	Phe	Ser
	210					215					220				
Glu	Val	Cys	Ser	His	Thr	Arg	Ala	Val	Ile	Tyr	Met	Ala	Glu	Cys	Ile
225					230					235					240
Lys	His	Glu	Cys	Cys	Leu	Ile	Gly	Ile	Pro	Arg	Ser	Lys	Ser	Ser	Gln
				245					250					255	
Pro	Ile	Ser	Arg	Cys	Thr	Lys	Gln	Glu	Cys	Val	Cys	Val	Gly	Leu	Asn
			260					265					270		
Ala	Lys	Lys	Tyr	Pro	Ser	Arg	Gly	Ser	Phe	Tyr	Val	Pro	Val	Glu	Ser
		275					280					285			
Thr	Ala	Pro	Phe	Cys	Asn	Asn	Lys	Gly	Lys	Ile	Ile				
	290					295					300				

<210> SEQ ID NO 165

<211> LENGTH: 204

<212> TYPE: PRT

<213> ORGANISM: Vespula maculifrons (Eastern yellow jacket) (Wasp)

<400> SEQUENCE: 165

Asn	Asn	Tyr	Cys	Lys	Ile	Lys	Cys	Leu	Lys	Gly	Gly	Val	His	Thr	Ala
1				5				10						15	
Cys	Lys	Tyr	Gly	Ser	Leu	Lys	Pro	Asn	Cys	Gly	Asn	Lys	Lys	Val	Val
			20					25					30		
Ser	Tyr	Gly	Leu	Thr	Lys	Gln	Glu	Lys	Gln	Asp	Ile	Leu	Lys	Glu	His
		35					40					45			
Asn	Asp	Phe	Arg	Gln	Lys	Ile	Ala	Arg	Gly	Leu	Glu	Thr	Arg	Gly	Asn
	50					55					60				
Pro	Gly	Pro	Gln	Pro	Pro	Ala	Lys	Asn	Met	Lys	Asn	Leu	Val	Trp	Ser
65					70					75				80	
Asp	Glu	Leu	Ala	Tyr	Ile	Ala	Gln	Val	Trp	Ala	Asn	Gln	Cys	Gln	Tyr
			85						90					95	
Gly	His	Asp	Thr	Cys	Arg	Asp	Val	Ala	Lys	Tyr	Gln	Val	Gly	Gln	Asn
			100					105					110		

-continued

Val Ala Leu Thr Gly Ser Thr Ala Ala Val Tyr Asn Asp Pro Val Lys
 115 120 125

Leu Val Lys Met Trp Glu Asp Glu Val Lys Asp Tyr Asn Pro Lys Lys
 130 135 140

Lys Phe Ser Glu Asn Asn Phe Leu Lys Ile Gly His Tyr Thr Gln Met
 145 150 155 160

Val Trp Ala Asn Thr Lys Glu Val Gly Cys Gly Ser Ile Lys Tyr Ile
 165 170 175

Gln Glu Asn Trp His Lys His Tyr Leu Val Cys Asn Tyr Gly Pro Ser
 180 185 190

Gly Asn Phe Gln Asn Glu Glu Leu Tyr Gln Thr Lys
 195 200

<210> SEQ ID NO 166
 <211> LENGTH: 204
 <212> TYPE: PRT
 <213> ORGANISM: *Vespula pensylvanica* (Western yellow jacket) (Wasp)

<400> SEQUENCE: 166

Asn Asn Tyr Cys Lys Ile Lys Cys Leu Lys Gly Gly Val His Thr Ala
 1 5 10 15

Cys Lys Tyr Gly Ser Leu Lys Pro Asn Cys Gly Asn Lys Ile Val Val
 20 25 30

Ser Tyr Gly Leu Thr Lys Glu Glu Lys Gln Asp Ile Leu Lys Glu His
 35 40 45

Asn Asp Phe Arg Gln Lys Ile Ala Arg Gly Leu Glu Thr Arg Gly Asn
 50 55 60

Pro Gly Pro Gln Pro Pro Ala Lys Asn Met Lys Asn Leu Val Trp Asn
 65 70 75 80

Asp Glu Leu Ala Tyr Val Ala Gln Val Trp Ala Asn Gln Cys Gln Tyr
 85 90 95

Gly His Asp Thr Cys Arg Asp Val Ala Lys Tyr Pro Val Gly Gln Asn
 100 105 110

Val Ala Leu Thr Gly Ser Thr Ala Asp Lys Tyr Asp Asn Pro Val Lys
 115 120 125

Leu Val Lys Met Trp Glu Asp Glu Val Lys Asp Tyr Asn Pro Lys Lys
 130 135 140

Lys Phe Ser Glu Asn Asn Phe Asn Lys Ile Gly His Tyr Thr Gln Met
 145 150 155 160

Val Trp Ala Asn Thr Lys Glu Ile Gly Cys Gly Ser Ile Lys Tyr Ile
 165 170 175

Gln Asn Glu Trp His Lys His Tyr Leu Val Cys Asn Tyr Gly Pro Ser
 180 185 190

Gly Asn Phe Gly Asn Glu Glu Leu Tyr Gln Thr Lys
 195 200

<210> SEQ ID NO 167
 <211> LENGTH: 205
 <212> TYPE: PRT
 <213> ORGANISM: *Vespula squamosa* (Southern yellow jacket) (Wasp)

<400> SEQUENCE: 167

Val Asp Tyr Cys Lys Ile Lys Cys Leu Lys Gly Gly Val His Thr Ala
 1 5 10 15

Cys Lys Tyr Gly Thr Ser Thr Lys Pro Asn Cys Gly Asn Met Val Val
 20 25 30

-continued

Lys Ser Tyr Gly Val Thr Gln Ala Glu Lys Gln Glu Ile Leu Lys Ile
 35 40 45
 His Asn Asp Phe Arg Asn Lys Val Ala Arg Gly Leu Glu Thr Arg Gly
 50 55 60
 Asn Pro Gly Pro Gln Pro Pro Ala Lys Asn Met Asn Asn Leu Val Trp
 65 70 75 80
 Asn Asn Glu Leu Ala Asn Ile Ala Gln Ile Trp Ala Ser Gln Cys Lys
 85 90 95
 Tyr Gly His Asp Thr Cys Lys Asp Thr Thr Lys Tyr Asn Val Gly Gln
 100 105 110
 Asn Ile Ala Val Ser Ser Ser Thr Ala Ala Val Tyr Glu Asn Val Gly
 115 120 125
 Asn Leu Val Lys Ala Trp Glu Asn Glu Val Lys Asp Phe Asn Pro Thr
 130 135 140
 Ile Ser Trp Glu Gln Asn Glu Phe Lys Lys Ile Gly His Tyr Thr Gln
 145 150 155 160
 Met Val Trp Ala Lys Thr Lys Glu Ile Gly Cys Gly Ser Ile Lys Tyr
 165 170 175
 Val Asp Asn Asn Trp Tyr Thr His Tyr Leu Val Cys Asn Tyr Gly Pro
 180 185 190
 Ala Gly Asn Phe Gly Asn Gln Glu Val Tyr Glu Arg Lys
 195 200 205

<210> SEQ ID NO 168

<211> LENGTH: 336

<212> TYPE: PRT

<213> ORGANISM: *Vespula vulgaris* (Yellow jacket) (Wasp)

<400> SEQUENCE: 168

Met Glu Glu Asn Met Asn Leu Lys Tyr Leu Leu Leu Phe Val Tyr Phe
 1 5 10 15
 Val Gln Val Leu Asn Cys Cys Tyr Gly His Gly Asp Pro Leu Ser Tyr
 20 25 30
 Glu Leu Asp Arg Gly Pro Lys Cys Pro Phe Asn Ser Asp Thr Val Ser
 35 40 45
 Ile Ile Ile Glu Thr Arg Glu Asn Arg Asn Arg Asp Leu Tyr Thr Leu
 50 55 60
 Gln Thr Leu Gln Asn His Pro Glu Phe Lys Lys Lys Thr Ile Thr Arg
 65 70 75 80
 Pro Val Val Phe Ile Thr His Gly Phe Thr Ser Ser Ala Ser Glu Thr
 85 90 95
 Asn Phe Ile Asn Leu Ala Lys Ala Leu Val Asp Lys Asp Asn Tyr Met
 100 105 110
 Val Ile Ser Ile Asp Trp Gln Thr Ala Ala Cys Thr Asn Glu Ala Ala
 115 120 125
 Gly Leu Lys Tyr Leu Tyr Tyr Pro Thr Ala Ala Arg Asn Thr Arg Leu
 130 135 140
 Val Gly Gln Tyr Ile Ala Thr Ile Thr Gln Lys Leu Val Lys His Tyr
 145 150 155 160
 Lys Ile Ser Met Ala Asn Ile Arg Leu Ile Gly His Ser Leu Gly Ala
 165 170 175
 His Ala Ser Gly Phe Ala Gly Lys Lys Val Gln Glu Leu Lys Leu Gly
 180 185 190
 Lys Tyr Ser Glu Ile Ile Gly Leu Asp Pro Ala Arg Pro Ser Phe Asp
 195 200 205

-continued

Ser Asn His Cys Ser Glu Arg Leu Cys Glu Thr Asp Ala Glu Tyr Val
 210 215 220

Gln Ile Ile His Thr Ser Asn Tyr Leu Gly Thr Glu Lys Thr Leu Gly
 225 230 235 240

Thr Val Asp Phe Tyr Met Asn Asn Gly Lys Asn Gln Pro Gly Cys Gly
 245 250 255

Arg Phe Phe Ser Glu Val Cys Ser His Ser Arg Ala Val Ile Tyr Met
 260 265 270

Ala Glu Cys Ile Lys His Glu Cys Cys Leu Ile Gly Ile Pro Lys Ser
 275 280 285

Lys Ser Ser Gln Pro Ile Ser Ser Cys Thr Lys Gln Glu Cys Val Cys
 290 295 300

Val Gly Leu Asn Ala Lys Lys Tyr Pro Ser Arg Gly Ser Phe Tyr Val
 305 310 315 320

Pro Val Glu Ser Thr Ala Pro Phe Cys Asn Asn Lys Gly Lys Ile Ile
 325 330 335

<210> SEQ ID NO 169
 <211> LENGTH: 331
 <212> TYPE: PRT
 <213> ORGANISM: *Vespula vulgaris* (Yellow jacket) (Wasp)

<400> SEQUENCE: 169

Ser Glu Arg Pro Lys Arg Val Phe Asn Ile Tyr Trp Asn Val Pro Thr
 1 5 10 15

Phe Met Cys His Gln Tyr Asp Leu Tyr Phe Asp Glu Val Thr Asn Phe
 20 25 30

Asn Ile Lys Arg Asn Ser Lys Asp Asp Phe Gln Gly Asp Lys Ile Ala
 35 40 45

Ile Phe Tyr Asp Pro Gly Glu Phe Pro Ala Leu Leu Ser Leu Lys Asp
 50 55 60

Gly Lys Tyr Lys Lys Arg Asn Gly Gly Val Pro Gln Glu Gly Asn Ile
 65 70 75 80

Thr Ile His Leu Gln Lys Phe Ile Glu Asn Leu Asp Lys Ile Tyr Pro
 85 90 95

Asn Arg Asn Phe Ser Gly Ile Gly Val Ile Asp Phe Glu Arg Trp Arg
 100 105 110

Pro Ile Phe Arg Gln Asn Trp Gly Asn Met Lys Ile His Lys Asn Phe
 115 120 125

Ser Ile Asp Leu Val Arg Asn Glu His Pro Thr Trp Asn Lys Lys Met
 130 135 140

Ile Glu Leu Glu Ala Ser Lys Arg Phe Glu Lys Tyr Ala Arg Phe Phe
 145 150 155 160

Met Glu Glu Thr Leu Lys Leu Ala Lys Lys Thr Arg Lys Gln Ala Asp
 165 170 175

Trp Gly Tyr Tyr Gly Tyr Pro Tyr Cys Phe Asn Met Ser Pro Asn Asn
 180 185 190

Leu Val Pro Glu Cys Asp Val Thr Ala Met His Glu Asn Asp Lys Met
 195 200 205

Ser Trp Leu Phe Asn Asn Gln Asn Val Leu Leu Pro Ser Val Tyr Val
 210 215 220

Arg Gln Glu Leu Thr Pro Asp Gln Arg Ile Gly Leu Val Gln Gly Arg
 225 230 235 240

Val Lys Glu Ala Val Arg Ile Ser Asn Asn Leu Lys His Ser Pro Lys

-continued

245				250				255							
Val	Leu	Ser	Tyr	Trp	Trp	Tyr	Val	Tyr	Gln	Asp	Glu	Thr	Asn	Thr	Phe
			260						265				270		
Leu	Thr	Glu	Thr	Asp	Val	Lys	Lys	Thr	Phe	Gln	Glu	Ile	Val	Ile	Asn
		275					280					285			
Gly	Gly	Asp	Gly	Ile	Ile	Ile	Trp	Gly	Ser	Ser	Ser	Asp	Val	Asn	Ser
	290					295					300				
Leu	Ser	Lys	Cys	Lys	Arg	Leu	Gln	Asp	Tyr	Leu	Leu	Thr	Val	Leu	Gly
305					310					315					320
Pro	Ile	Ala	Ile	Asn	Val	Thr	Glu	Ala	Val	Asn					
				325					330						

<210> SEQ ID NO 170

<211> LENGTH: 227

<212> TYPE: PRT

<213> ORGANISM: *Vespula vulgaris* (Yellow jacket) (Wasp)

<400> SEQUENCE: 170

Met	Glu	Ile	Ser	Gly	Leu	Val	Tyr	Leu	Ile	Ile	Ile	Val	Thr	Ile	Ile
1				5					10					15	
Asp	Leu	Pro	Tyr	Gly	Lys	Ala	Asn	Asn	Tyr	Cys	Lys	Ile	Lys	Cys	Leu
			20						25				30		
Lys	Gly	Gly	Val	His	Thr	Ala	Cys	Lys	Tyr	Gly	Ser	Leu	Lys	Pro	Asn
		35					40					45			
Cys	Gly	Asn	Lys	Val	Val	Val	Ser	Tyr	Gly	Leu	Thr	Lys	Gln	Glu	Lys
	50					55					60				
Gln	Asp	Ile	Leu	Lys	Glu	His	Asn	Asp	Phe	Arg	Gln	Lys	Ile	Ala	Arg
65					70				75						80
Gly	Leu	Glu	Thr	Arg	Gly	Asn	Pro	Gly	Pro	Gln	Pro	Pro	Ala	Lys	Asn
				85					90					95	
Met	Lys	Asn	Leu	Val	Trp	Asn	Asp	Glu	Leu	Ala	Tyr	Val	Ala	Gln	Val
			100						105				110		
Trp	Ala	Asn	Gln	Cys	Gln	Tyr	Gly	His	Asp	Thr	Cys	Arg	Asp	Val	Ala
		115					120					125			
Lys	Tyr	Gln	Val	Gly	Gln	Asn	Val	Ala	Leu	Thr	Gly	Ser	Thr	Ala	Ala
	130					135					140				
Lys	Tyr	Asp	Asp	Pro	Val	Lys	Leu	Val	Lys	Met	Trp	Glu	Asp	Glu	Val
145					150					155					160
Lys	Asp	Tyr	Asn	Pro	Lys	Lys	Lys	Phe	Ser	Gly	Asn	Asp	Phe	Leu	Lys
				165					170					175	
Thr	Gly	His	Tyr	Thr	Gln	Met	Val	Trp	Ala	Asn	Thr	Lys	Glu	Val	Gly
		180							185				190		
Cys	Gly	Ser	Ile	Lys	Tyr	Ile	Gln	Glu	Lys	Trp	His	Lys	His	Tyr	Leu
		195					200					205			
Val	Cys	Asn	Tyr	Gly	Pro	Ser	Gly	Asn	Phe	Met	Asn	Glu	Glu	Leu	Tyr
		210				215					220				
Gln	Thr	Lys													
225															

<210> SEQ ID NO 171

<211> LENGTH: 206

<212> TYPE: PRT

<213> ORGANISM: *Vespula vidua* (Yellow jacket) (Wasp)

<400> SEQUENCE: 171

Lys Val Asn Tyr Cys Lys Ile Lys Cys Leu Lys Gly Gly Val His Thr

-continued

1	5	10	15
Ala Cys Lys Tyr Gly Thr Ser Thr Lys Pro Asn Cys Gly Lys Met Val	20	25	30
Val Lys Ala Tyr Gly Leu Thr Glu Ala Glu Lys Gln Glu Ile Leu Lys	35	40	45
Val His Asn Asp Phe Arg Gln Lys Val Ala Lys Gly Leu Glu Thr Arg	50	55	60
Gly Asn Pro Gly Pro Gln Pro Pro Ala Lys Asn Met Asn Asn Leu Val	65	70	75
Trp Asn Asp Glu Leu Ala Asn Ile Ala Gln Val Trp Ala Ser Gln Cys	85	90	95
Asn Tyr Gly His Asp Thr Cys Lys Asp Thr Glu Lys Tyr Pro Val Gly	100	105	110
Gln Asn Ile Ala Lys Arg Ser Thr Thr Ala Ala Leu Phe Asp Ser Pro	115	120	125
Gly Lys Leu Val Lys Met Trp Glu Asn Glu Val Lys Asp Phe Asn Pro	130	135	140
Asn Ile Glu Trp Ser Lys Asn Asn Leu Lys Lys Thr Gly His Tyr Thr	145	150	155
Gln Met Val Trp Ala Lys Thr Lys Glu Ile Gly Cys Gly Ser Val Lys	165	170	175
Tyr Val Lys Asp Glu Trp Tyr Thr His Tyr Leu Val Cys Asn Tyr Gly	180	185	190
Pro Ser Gly Asn Phe Arg Asn Glu Lys Leu Tyr Glu Lys Lys	195	200	205

<210> SEQ ID NO 172

<211> LENGTH: 202

<212> TYPE: PRT

<213> ORGANISM: Vespa mandarinia (Hornet)

<400> SEQUENCE: 172

Asn Asn Tyr Cys Lys Ile Lys Cys Arg Ser Gly Ile His Thr Leu Cys	1	5	10	15
Lys Phe Gly Ile Ser Thr Lys Pro Asn Cys Gly Lys Asn Val Val Lys	20	25	30	
Ala Ser Gly Leu Thr Lys Ala Glu Lys Leu Glu Ile Leu Lys Gln His	35	40	45	
Asn Glu Phe Arg Gln Lys Val Ala Arg Gly Leu Glu Thr Arg Gly Lys	50	55	60	
Pro Gly Pro Gln Pro Pro Ala Lys Ser Met Asn Thr Leu Val Trp Asn	65	70	75	80
Asp Glu Leu Ala Gln Ile Ala Gln Val Trp Ala Gly Gln Cys Asp Tyr	85	90	95	
Gly His Asp Val Cys Arg Asn Thr Ala Lys Tyr Ser Val Gly Gln Asn	100	105	110	
Ile Ala Glu Asn Gly Ser Thr Ala Ala Ser Phe Ala Ser Val Ser Asn	115	120	125	
Met Val Gln Met Trp Ala Asp Glu Val Lys Asn Tyr Gln Tyr Gly Ser	130	135	140	
Thr Lys Asn Lys Leu Ile Glu Val Gly His Tyr Thr Gln Met Val Trp	145	150	155	160
Ala Lys Thr Lys Glu Ile Gly Cys Gly Ser Ile Lys Tyr Ile Glu Asn	165	170	175	

-continued

Gly Trp His Arg His Tyr Leu Val Cys Asn Tyr Gly Pro Ala Gly Asn
 180 185 190

Ile Gly Asn Glu Pro Ile Tyr Glu Arg Lys
 195 200

<210> SEQ ID NO 173
 <211> LENGTH: 191
 <212> TYPE: PRT
 <213> ORGANISM: Zea mays (Maize)

<400> SEQUENCE: 173

Met Thr Ala Cys Gly Asn Val Pro Ile Phe Lys Asp Gly Lys Gly Cys
 1 5 10 15

Gly Ser Cys Tyr Glu Val Arg Cys Lys Glu Lys Pro Glu Cys Ser Gly
 20 25 30

Asn Pro Val Thr Val Phe Ile Thr Asp Met Asn Tyr Glu Pro Ile Ala
 35 40 45

Pro Tyr His Phe Asp Leu Ser Gly Lys Ala Phe Gly Ser Leu Ala Lys
 50 55 60

Pro Gly Leu Asn Asp Lys Leu Arg His Cys Gly Ile Met Asp Val Glu
 65 70 75 80

Phe Arg Arg Val Arg Cys Lys Tyr Pro Ala Gly Gln Lys Ile Val Phe
 85 90 95

His Ile Glu Lys Gly Cys Asn Pro Asn Tyr Val Ala Val Leu Val Lys
 100 105 110

Phe Val Ala Asp Asp Gly Asp Ile Val Leu Met Glu Ile Gln Asp Lys
 115 120 125

Leu Ser Ala Glu Trp Lys Pro Met Lys Leu Ser Trp Gly Ala Ile Trp
 130 135 140

Arg Met Asp Thr Ala Lys Ala Leu Lys Gly Pro Phe Ser Ile Arg Leu
 145 150 155 160

Thr Ser Glu Ser Gly Lys Lys Val Ile Ala Lys Asp Ile Ile Pro Ala
 165 170 175

Asn Trp Arg Pro Asp Ala Val Tyr Thr Ser Asn Val Gln Phe Tyr
 180 185 190

<210> SEQ ID NO 174
 <211> LENGTH: 73
 <212> TYPE: DNA
 <213> ORGANISM: Unknown
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence

<400> SEQUENCE: 174

gctcgagggt ggagcgggt caggcggagg tggctctggc ggtggcggat cgttcacccc 60

gcccaccgtg aag 73

<210> SEQ ID NO 175
 <211> LENGTH: 33
 <212> TYPE: DNA
 <213> ORGANISM: Unknown
 <220> FEATURE:
 <223> OTHER INFORMATION: Primer sequence

<400> SEQUENCE: 175

ggcggccgct cattaccgg gatttacaga cac 33

<210> SEQ ID NO 176
 <211> LENGTH: 32

-continued

<212> TYPE: PRT
 <213> ORGANISM: Arachis hypogaea (peanut)
 <220> FEATURE:
 <221> NAME/KEY: UNSURE
 <222> LOCATION: 1, 4, 11, 12, 27, 30
 <223> OTHER INFORMATION: Xaa = any amino acid
 <400> SEQUENCE: 176

Xaa Gln Gln Xaa Glu Leu Gln Asp Leu Glu Xaa Xaa Gln Ser Gln Leu
 1 5 10 15
 Glu Asp Ala Asn Leu Arg Pro Arg Glu Gln Xaa Leu Met Xaa Lys Ile
 20 25 30

<210> SEQ ID NO 177
 <211> LENGTH: 32
 <212> TYPE: PRT
 <213> ORGANISM: Arachis hypogaea (peanut)
 <220> FEATURE:
 <221> NAME/KEY: UNSURE
 <222> LOCATION: 1, 4, 8, 10, 11, 12, 27, 30
 <223> OTHER INFORMATION: Xaa = any amino acid

<400> SEQUENCE: 177
 Xaa Gln Gln Xaa Glu Leu Gln Xaa Asp Xaa Xaa Xaa Gln Ser Gln Leu
 1 5 10 15
 Glu Arg Ala Asp Leu Arg Pro Gly Glu Gln Xaa Leu Met Xaa Lys Ile
 20 25 30

What is claimed is:

1. An isolated fusion molecule comprising a first polypeptide sequence consisting of the amino acid sequence of SEQ ID NO: 3 and being capable of specific binding to a native IgG inhibitory receptor comprising an immune receptor tyrosine-based inhibitory motif (ITIM), expressed on mast cells, basophils or B cells, said first polypeptide sequence being functionally connected with a polypeptide linker of between about 5 to 25 amino acids to a second polypeptide sequence consisting of a native allergen polypeptide sequence selected from SEQ ID NOs: 8 through 173, said second polypeptide sequence being capable of specific binding indirectly to a native IgE receptor (FcεR), wherein said polypeptide linker allows said first polypeptide and said second polypeptide to independently assume a tertiary conformation effective to allow binding with a native receptor, and wherein said isolated fusion molecule is capable of cross-linking said native IgG inhibitory receptor and said native IgE receptor.

2. The fusion molecule of claim 1 wherein said inhibitory receptor is a low-affinity IgG receptor FcγRIIb.

3. The fusion molecule of claim 2 wherein said IgE receptor is a high-affinity FcεRI receptor.

4. The fusion molecule of claim 2 wherein said IgE receptor is a low-affinity IgE receptor FcεRII (CD23).

5. The fusion molecule of claim 3 wherein said FcγRIIb and FcεRI receptors are of human origin.

6. The fusion molecule of claim 4 wherein said FcγRIIb and FcεRII receptors are of human origin.

7. The fusion molecule of claim 1 wherein said allergen sequence is that of a food allergen.

8. The fusion molecule of claim 7 wherein said food allergen is selected from the group consisting of peanut, shellfish, milk, fish, soy, wheat, egg and tree nut allergens.

9. The fusion molecule of claim 1 wherein said allergen sequence is that of a pollen allergen.

10. The fusion molecule of claim 1 wherein said IgE receptor is a high-affinity FcεRI receptor.

11. The fusion molecule of claim 1 wherein said native IgE receptor is a low-affinity FcεRII receptor (CD23).

12. The fusion molecule of claim 1 wherein said IgG inhibitory receptor is a low affinity FcγRIIb receptor.

13. The fusion molecule of claim 12 wherein said IgE receptor is a high-affinity FcεRI receptor.

14. The fusion molecule of claim 13 wherein said FcγRIIb and FcεRI receptors are of human origin.

15. The fusion molecule of claim 1 wherein said polypeptide linker consists of 10 to 25 amino acid residues.

16. The fusion molecule of claim 15 wherein said polypeptide linker consists of 15 to 25 amino acid residues.

17. An isolated fusion molecule consisting of a first polypeptide sequence encoded by nucleic acid of SEQ ID NO: 1, wherein said first polypeptide sequence is capable of specific binding to a native human FcγRIIb receptor, and said first polypeptide sequence being functionally connected with a polypeptide linker of between about 5 to 25 amino acids to a second polypeptide sequence consisting of a native allergen polypeptide sequence selected from SEQ ID NOs: 8 through 173, said second polypeptide sequence being capable of specific binding indirectly to a high-affinity FcεRI receptor, wherein said polypeptide linker allows said first polypeptide and said second polypeptide to independently assume a tertiary conformation effective to allow binding with a native receptor, and wherein said isolated fusion molecule is capable of cross-linking said native IgG inhibitory receptor and said high-affinity FcεRI receptor.

18. A pharmaceutical composition comprising the fusion molecule of claim 1 in admixture with a pharmaceutically acceptable ingredient.

19. A pharmaceutical composition comprising the fusion molecule of claim 3 in admixture with a pharmaceutically acceptable ingredient.

263

20. An article of manufacture comprising a container, the fusion molecule of claim **1** within the container, and a label or package insert on or associated with the container.

21. The article of manufacture of claim **20** wherein said label or package insert comprises instructions for the treatment of an IgE-mediated biological response. 5

22. The article of manufacture of claim **21** wherein said biological response is a mediated hypersensitivity reaction.

23. The article of manufacture of claim **22** wherein said label or package insert contains instruction for the treatment

264

of a condition selected from the group consisting of asthma, allergic rhinitis, atopic dermatitis, severe food allergies, chronic urticaria, angioedema, and anaphylactic shock.

24. The isolated fusion molecule of claim **1**, wherein said first polypeptide consisting of the γ -hinge-CH2-CH3 domain of a native IgG immunoglobulin heavy chain constant region and consisting of the amino acid sequence of SEQ ID NO: 3.

* * * * *